

Figure 1
Sequence of human APRIL (SEQ ID NOS: 1 and 2)

Human G70 cDNA (SEQ ID NO 1)

Length: 1465 bp

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1  GCCAACCTTC GCTGCCCCAA CCCTGGGGCC GCCCCAGGGT TCCTGCGCAC
51  TGCCTGTTCC TCCTGGGTGT CACTGGCAGC CCTGTCCTTC CTAGAGGGAC
101  TGGAACTTAA TTCTCCTGAG GCTGAGGGAG GGTGGAGGGT CTCAAGGCAA
151  CGCTGGCCCC ACGACGGAGT GCCAGGAGCA CTAACAGTAC CCTTAGCTTG
201  CTTTCCTCCT CCTTCCTFFT TATTTTCAAG TTCCTTTTTA TTTCTCCTTG
251  CGTAACAACC TTCTTCCCTT CTGCACCACT GCCCGTACCC TTACCCGCCG
301  CGCCACCTCC TTGCTACCCC ACTCTTGAAA CCACAGCTGT TGGCAGGGTC
351  CCCAGCTCAT GCCAGCCTCA TCTCCTTTCT TGCTAGCCCC CAAAGGGCCT
401  CCAGGCAACA TGGGGGGCCC AGTCAGAGAG CCGGCACTCT CAGTTGCCCT
451  CTGGTTGAGT TGGGGGGCAG CTCTGGGGGC CGTGGCTTGT GCCATGGCTC
501  TGCTGACCCA ACAAACAGAG CTGCAGAGCC TCAGGAGAGA GGTGAGCCGG
551  CTGCAGGGGA CAGGAGGCCC CTCCCAGAAT GGGGAAGGGT ATCCCTGGCA
601  GAGTCTCCCG GAGCAGAGTT CCGATGCCCT GGAAGCCTGG GAGAGTGGGG
651  AGAGATCCCG GAAAAGGAGA GCAGTGCTCA CCCAAAAACA GAAGAAGCAG
701  CACTCTGTCC TGCACCTGGT TCCCATTAA CACACCTCCA AGGATGACTC
751  CGATGTGACA GAGGTGATGT GGCAACCAGC TCTTAGGCGT GGGAGAGGCC
801  TACAGGCCCA AGGATATGGT GTCCGAATCC AGGATGCTGG AGTTTATCTG
851  CTGTATAGCC AGGTCTGTGT TCAAGACGTG ACTTTCACCA TGGGTCAGGT
901  GGTGTCTCGA GAAGGCCAAG GAAGGCAGGA GACTCTATTC CGATGTATAA
951  GAAGTATGCC CTCCCACCCG GACCGGGCCT ACAACAGCTG CTATAGCGCA
1001  GGTGTCTTCC ATTTACACCA AGGGGATATT CTGAGTGTC AATTCCCCG
1051  GGCAAGGGCG AACTTAAACC TCTCTCCACA TGAACCTTC CTGGGGTTTG
1101  TGAAACTGTG ATTGTGTTAT AAAAAGTGGC TCCAGCTTG GAAGACCAGG
1151  GTGGGTACAT ACTGGAGACA GCCAAGAGCT GAGTATATAA AGGAGAGGGA
1201  ATGTGCAGGA ACAGAGGCGT CTTCTGGGT TTGGCTCCCC GTTCCTCACT
1251  TTTCCCTTTT CATTCCACC CCCTAGACTT TGATTTTACG GATATCTTGC
1301  TTCTGTTCCC CATGGAGCTC CGAATCTTG CGTGTGTGTA GATGAGGGGC
1351  GGGGGACGGG CGCCAGGCAT TGTTCAAGAC TGGTCGGGGC CCACTGGAAG
1401  CATCCAGAAC AGCACCACCA TCTAACGGCC GCTCGAGGGA AGCACC CGC
1451  GGTTTGGGCG AAGTC

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The proposed transmembrane domains are boxed

human G70 protein sequence (SEQ ID NO 2)

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1  MPASSPFLLA PKGPPGNMGG PVREPALSA LWLSWGAALG AVACAMALLT
51  QQTELQSLRR EVSRLQGTGG PSQNGEGYPW QSLPEQSSDA LEAWESGERS
101  RKRRAVLTQK QKKQHSVLHL VPINATSKDD SDVTEVMWQP ALRRGRGLQA
151  QGYGVRIQDA GVYLLYSQVL FQDVTFTMGQ VVSREGQGRQ ETLFR CIRSM
201  PSHPDRA YNS CYSAGVFHLH QGDILSVIIP RARAKLNLSP HGTFLG FVKL

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Figure 2A
Sequence of mouse G70 (SEQ ID NOS: 3 and 4)

Mouse G70 (SEQ ID NO 3)

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1  CATGCCGAGT GCTTTGTGTG TGTTACCTGC TCTAAGAAGC TGGCTGGGCA
51  GCGTTTCACC GCTGTGGAGG ACCAGTATTA CTGCGTGGAT TGCTACAAGA
101 ACTTTGTGGC CAAGAAGTGT GCTGGATGCA AGAACCCCAT CACTGGGTTT
151 GGTAAGGCT CCAGTGTGGT GGCCTATGAA GGACAATCCT GGCACGACTA
201 CTGCTTCCAC TGCAAAAAAT GCTCCGTGAA TCTGGCCAAC AAGCGCTTTG
251 TATTTCATAA TGAGCAGGTG TATTGCCCTG ACTGTGCCAA AAAGCTGTAA
301 CTTGACGGCT GCCCTGTCCT TCCTAGATAA TGGCACCAAA TTCTCCTGAG
351 GCTAGGGGGG AAGGAGTGTC AGAGTGTAC TAGCTCGACC CTGGGGACAA
401 GGGGGACTAA TAGTACCCTA GCTTGATTTT TTCCTATTCT CAAGTTCCTT
451 TTTATTTCTC CTTTGCCTAA CCCGCTCTTC CTTTCTGTGC CTTTGCCTGT
501 ATTCCCACCC TCCCTGCTAC CTCTTGGCCA CCTCACTTCT GAGACCACAG
551 CTGTTGGCAG GGTCCCTAGC TCATGCCAGC CTCATCTCCA GGCCACATGG
601 GGGGCTCAGT CAGAGAGCCA GCCCTTTCGG TTGCTCTTTG GTTGAGTTGG
651 GGGGCAGTTC TGGGGGCTGT GACTTGTGCT GTCGCACTAC TGATCCAACA
701 GACAGAGCTG CAAAGCCTAA GGCGGGAGGT GAGCCGGCTG CAGCGGAGTG
751 GAGGGCCTTC CCAGAAGCAG GGAGAGCGCC CATGGCAGAG CCTCTGGGAG
801 CAGAGTCCTG ATGTCTGGA AGCCTGGAAG GATGGGGCGA AATCTCGGAG
851 AAGGAGAGCA GTAATCACCC AGAAGCACAA GAAGAAGCAC TCAGTCCTGC
901 ATCTTGTTC AGTTAACATT ACCTCCAAGG ACTCTGACGT GACAGAGGTG
951 ATGTGGCAAC CAGTACTTAG GCGTGGGAGA GGCCTGGAGG CCCAGGGAGA
1001 CATGTACGA GTCTGGGACA CTGGAATTTA TCTGCTCTAT AGTCAGGTCC
1051 TGTTTCATGA TGTGACTTTC ACAATGGGTC AGGTGGTATC TCGGGAAGGA
1101 CAAGGGAGAA GAGAACTCT ATTCCGATGT ATCAGAAGTA TGCCTTCTGA
1151 TCCTGACCGT GCCTACAATA GCTGCTACAG TGCAGGTGTC TTTCATTTAC
1201 ATCAAGGGGA TATTATCACT GTCAAAATTC CACGGGCAA CGCAAACTT
1251 AGCCTTTCTC CGCATGGAAC ATTCCTGGGG TTTGTGAAAC TATGATTGTT
1301 ATAAAGGGGG TGGGGATTTT CCATTCCAAA AACTGGCTAG ACAAAGGACA
1351 AGGAACGGTC AAGAACAGCT CTCCATGGCT TTGCCTTGAC TGTTGTTCCT
1401 CCCTTTGCCT TTCCCGCTCC CACTATCTGG GCTTTGACTC CATGGATATT
1451 AAAAAAGTAG AATATTTTGT GTTTATCTCC CAAAAA
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Figure 2B

Mouse G70 Length: 241 (SEQ ID NO 4)

```
1  MPASSPGHMG GSVREPALSV ALWLSWGA VL GAVTCAVALL IQOTELQSLR
51  REVSRLQRSG GPSQKQGERP WQSLWEQSPD VLEAWKDGA K SRRRAVL TQ
101 KHKKKH SVLH LVPVNITSKD SDVTEVMWQP VLRRGRGLEA QGDIVRVWDT
151 GIYLLYSQVL FHDVTFTMGQ VVSREGQGR ETLFRCIRSM PSDPDRA YNS
201 CYSAGVFHLH QGDIITVKIP RANAKLSLSP HGTFLGFVKL *
```

G-70 FLAG des92 (smuG70) Strain #4081 (SEQ ID NO 19):

```
MDYKDDDDKKHKKKHSVLHLVPVNITSKDS DVTEVMWQPV LRRGRGLEA QGDIVRVW
DTGIYLLYSQVLFHDVTFTMGQVVSREGQGR ETLFRCIRSM PSDPDRA YNSCYSAG
VFHLHQGDIITVKIPRANAKLSLSPHGTFLGFVKL*
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Figure 3
Alignm. of human and mouse G70

mouse: 1	MPASS-----PGHMGGS	VREPALSVALWLSWGA	VLGAVTCAVALL	IQQTEQLSLRR	51
	MPASS	PG+MGG	VREPALSVALWLSWGA	LGAV CA+ALL	QQTEQLSLRR
Human: 1	MPASSPFLAPKGPPGNMGGP	VREPALSVALWLSWGA	AALGAVACAMALL	IQQTEQLSLRR	60
mouse: 52	EVSRLQRSGGPSQKQGER	PWQSLWEQSPDVLEAWKD	GAKSRRRAVL	TQKHKKKHSVLHL	111
	EVSRLQ +GGPSQ	PWQSL EQS D LEAW+ G	+SR+RAVL	TQK KK+HSVLHL	
human: 61	EVSRLQGTGGPSQNGEGYPWQSL	PEQSSDALEAWESGERSR	KRAVL	TQKQKKQHSLHL	120
mouse: 112	VPVNITSKD-SDVTEVMWQP	VLRGRGLEAQGDIVRVWD	TGIYLLYSQVLF	HDTVFTMGQ	170
	VP+N TSKD SDVTEVMWQP	LRRGRGL+AQG VR+ D	G+YLLYSQVLF	DVTFTMGQ	
human: 121	VPINATSKDDSDVTEVMWQP	PALRRGRGLQAQGYGVRIQ	DAGVYLLYSQVLF	QDVTFTMGQ	180
mouse: 171	VVSREGQGRRETLFRCIRSMPS	DPDRAYNSCYSAGVFHLH	QGDIIITVKIPRANAKLSLSP	230	
	VVSREGQGR+ETLFRCIRSMPS	PDRAYNSCYSAGVFHLH	QGDII+V IPRA AKL+LSP		
human: 181	VVSREGQGRQETLFRCIRSMPS	HPDRAYNSCYSAGVFHLH	QGDILSVIIPRARAKLNLSP	240	
mouse: 231	HGTFLGFVKL	240			
	HGTFLGFVKL				
human: 241	HGTFLGFVKL	250			

Effect of sG70/April on Raji cell proliferation

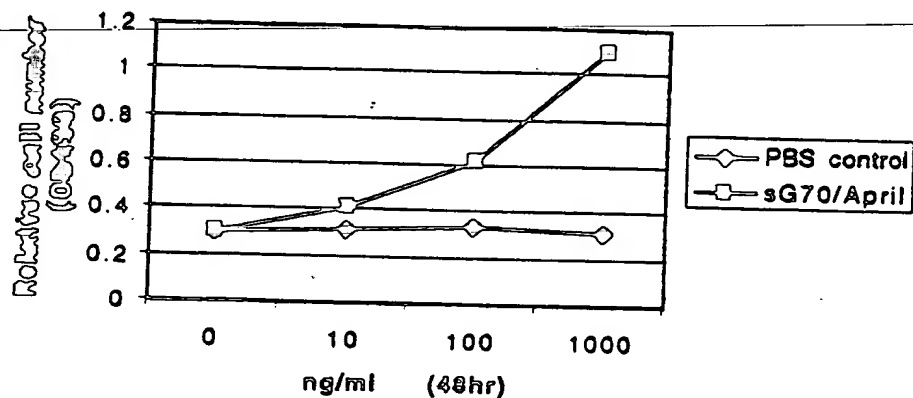
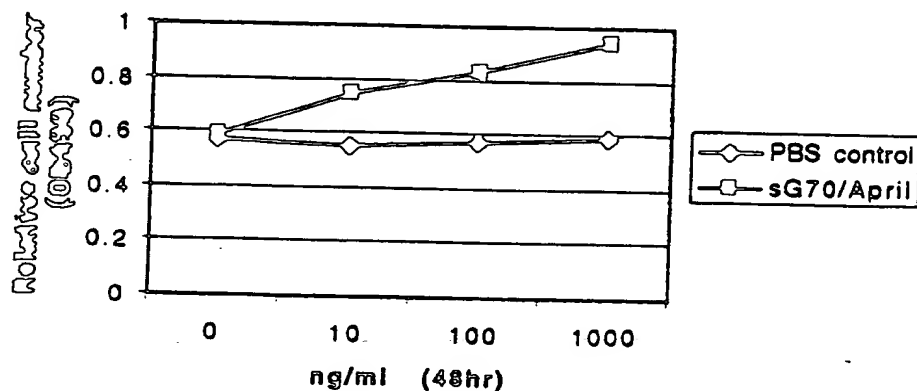


Fig. 4A

Effect of sG70/April on Jurkat cell proliferation



Effect of sG70/April on K562 cell proliferation

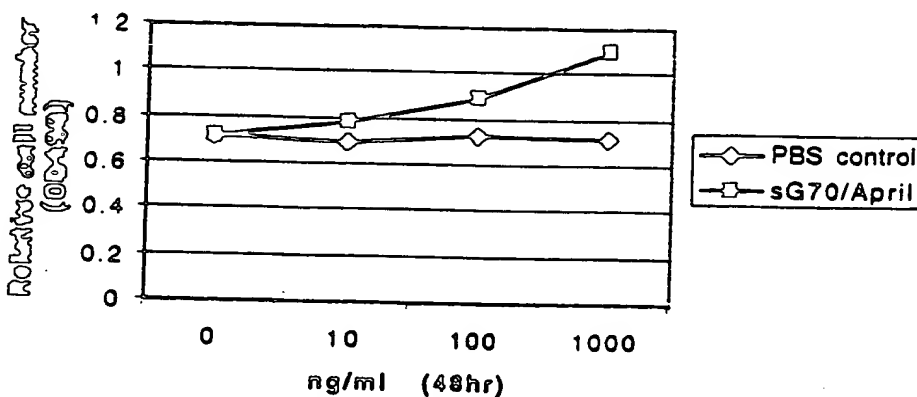


Fig. 4B

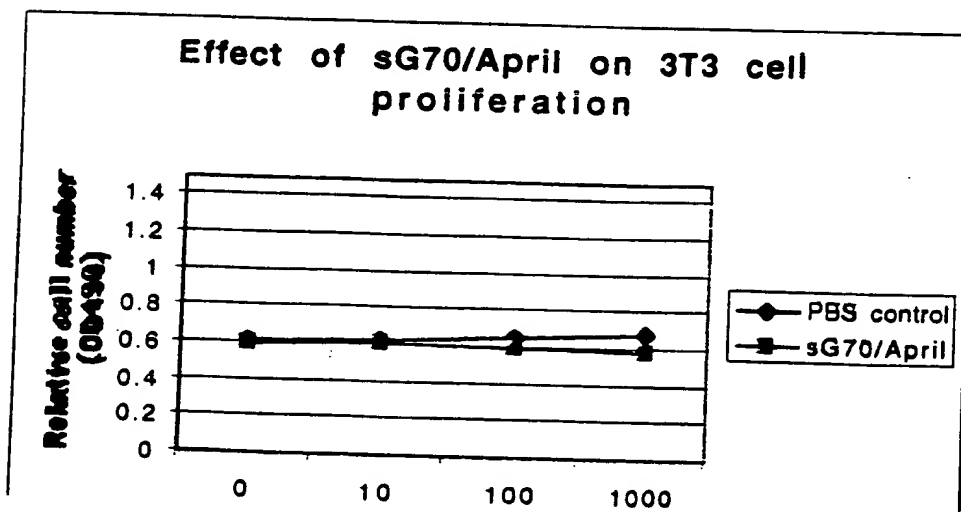
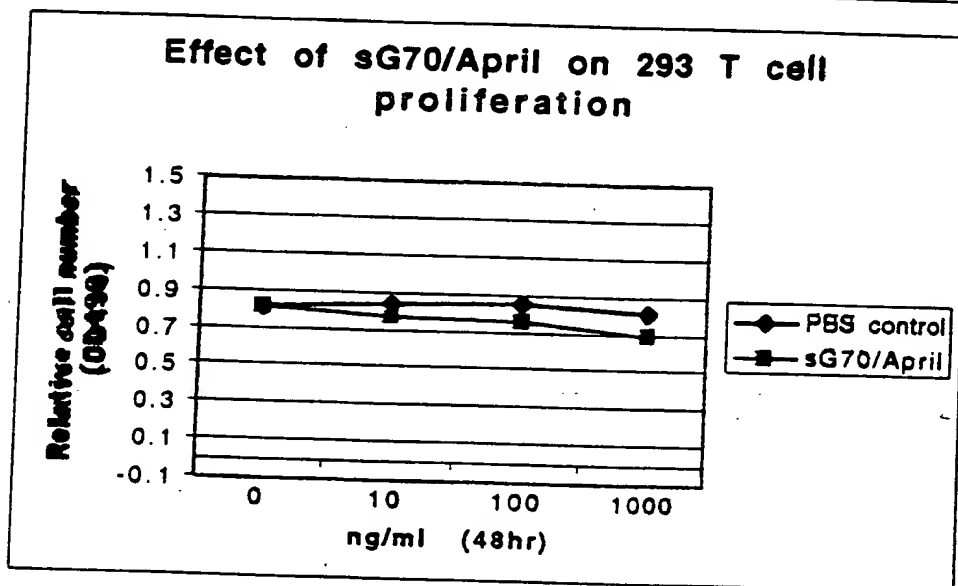
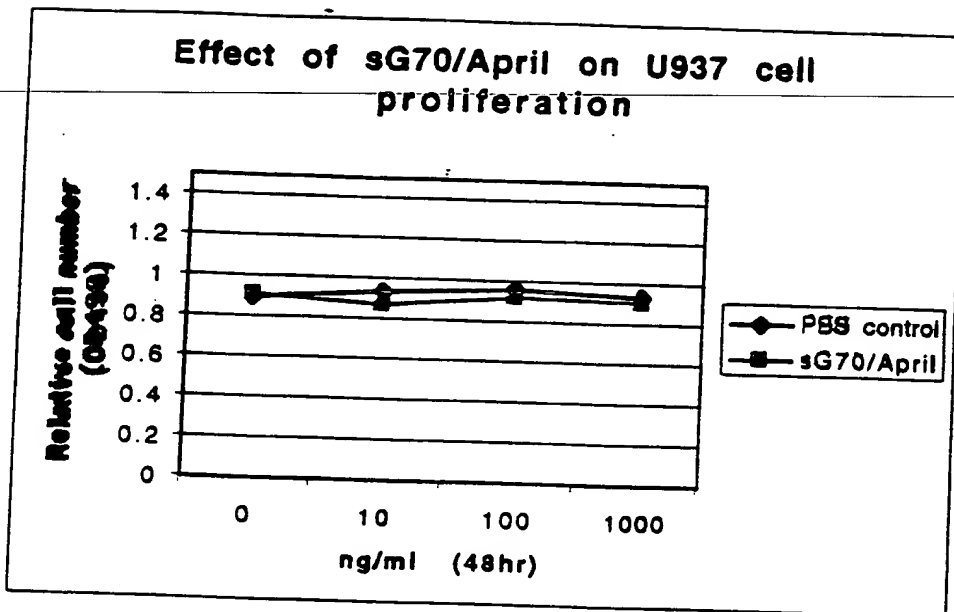
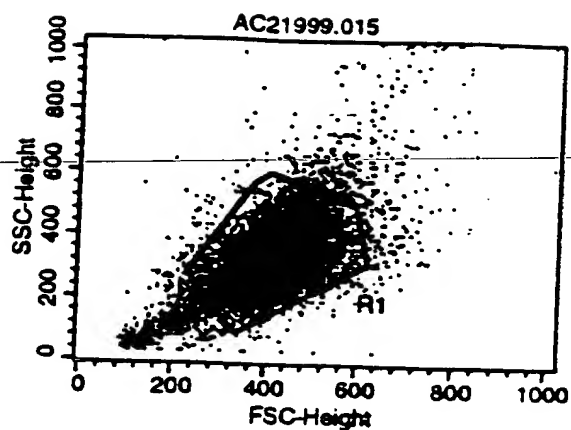


FIGURE 5A



FACS analysis of G70/April receptor binding

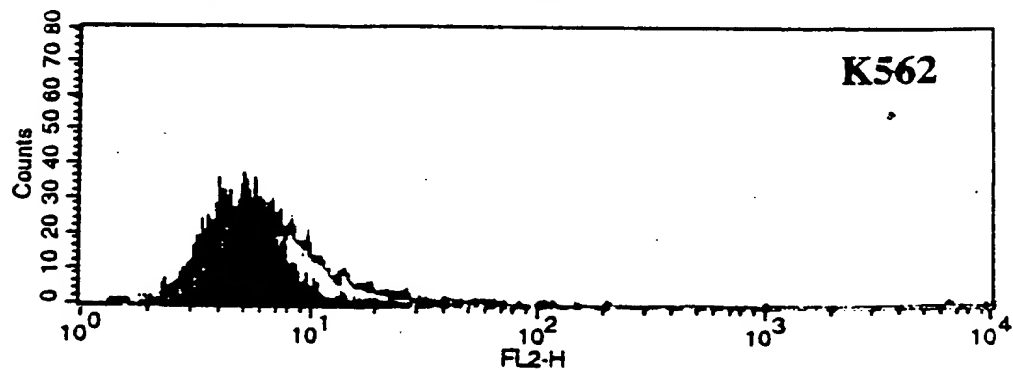
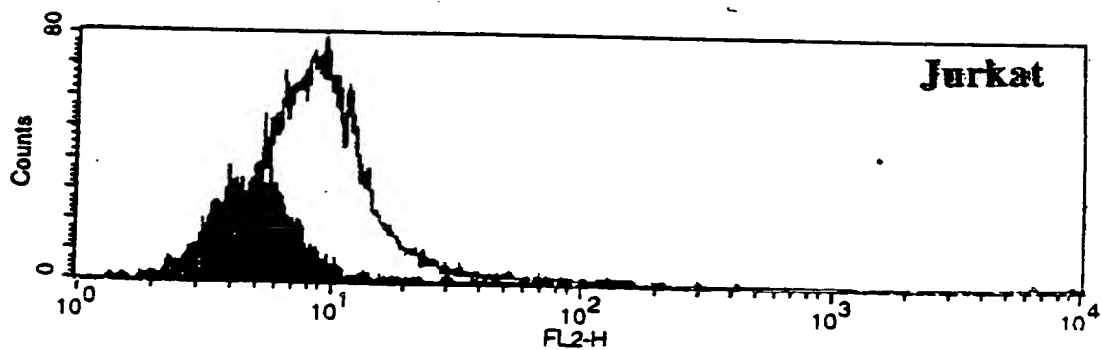
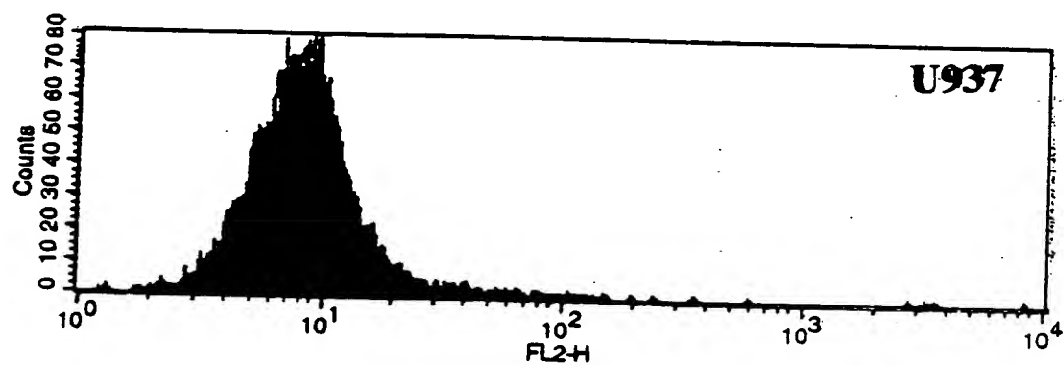
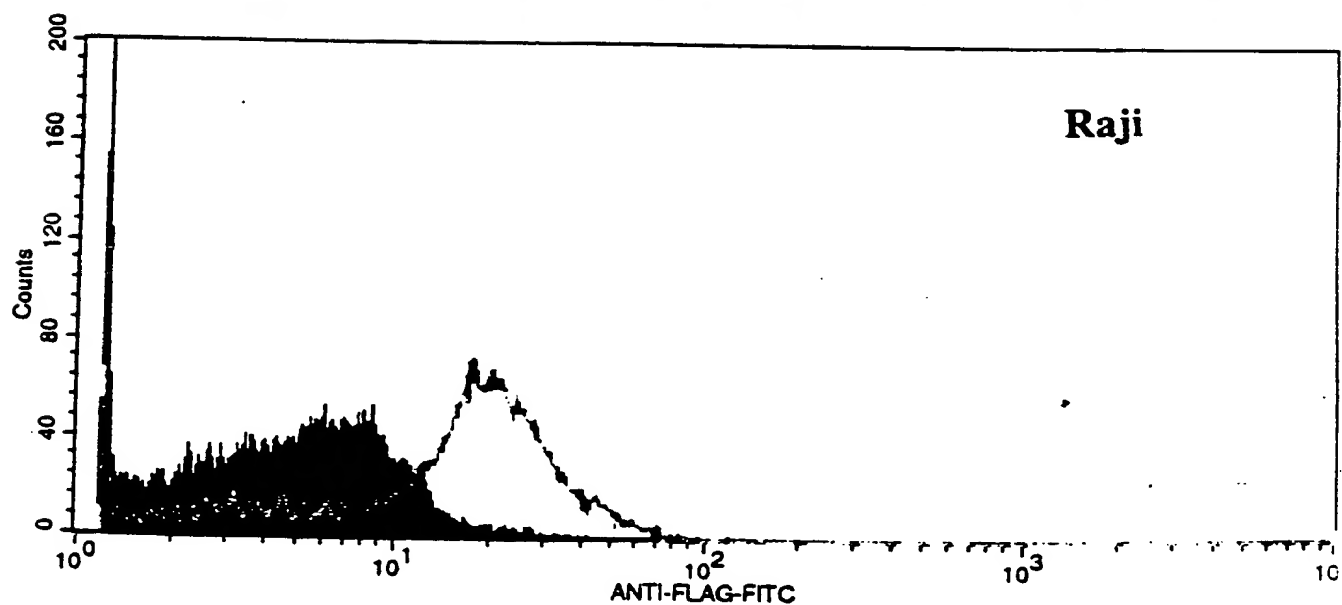
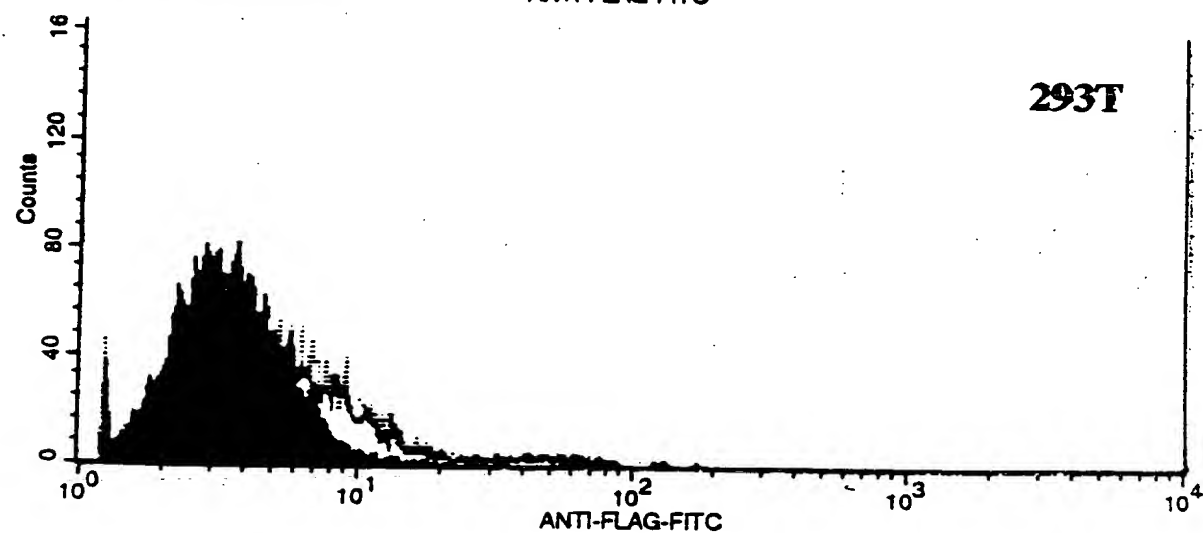
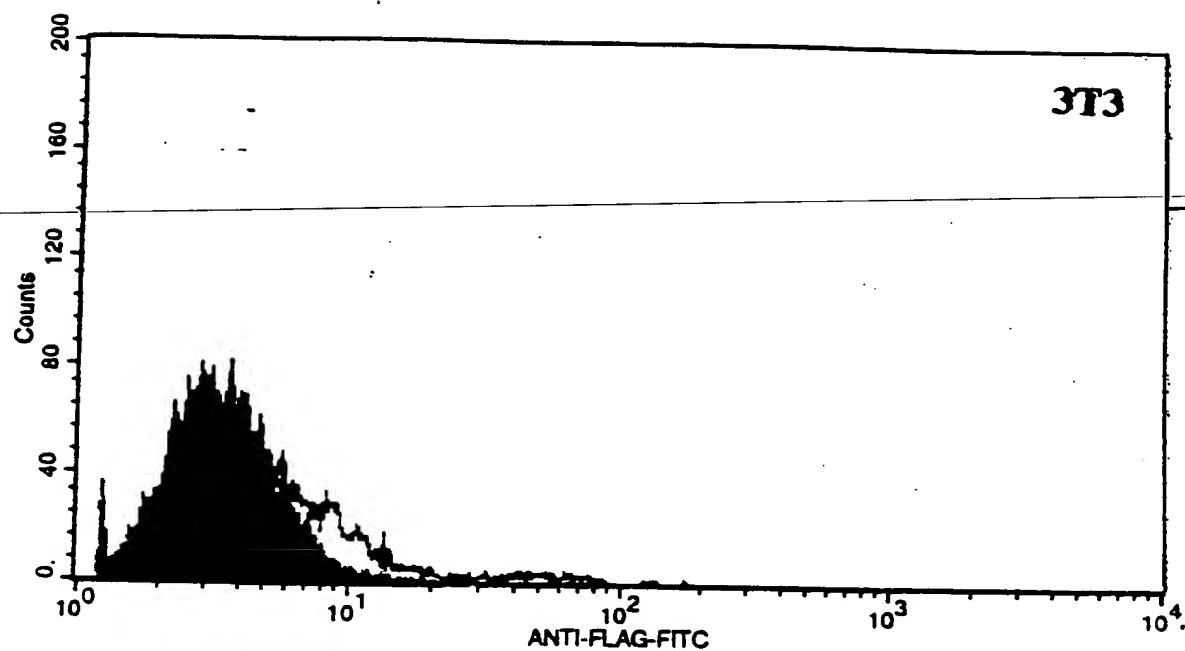


FIGURE 5B



The effect of r-G70/April on human peripheral blood B cell, T cell and Granulocyte

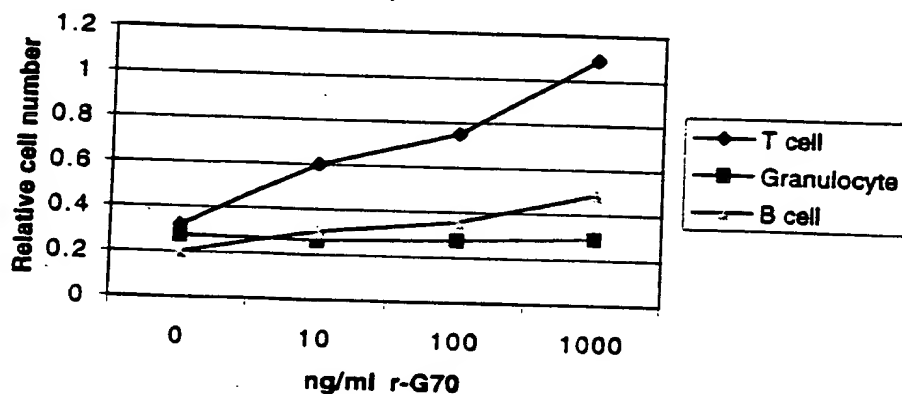
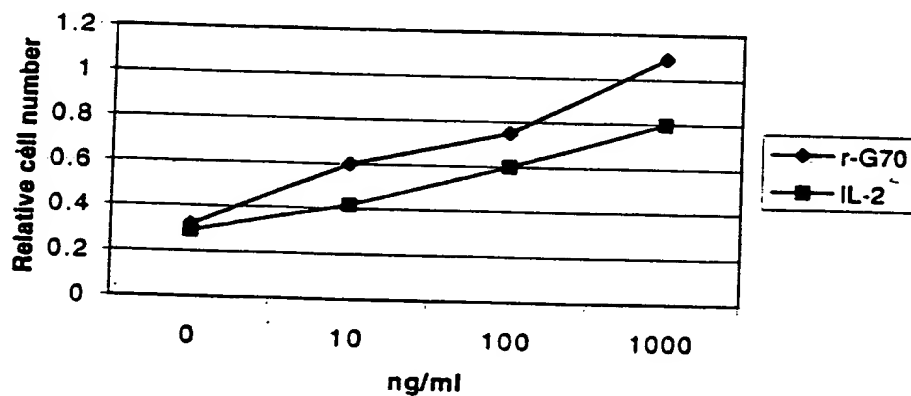


Fig. 6

The effect of IL-2 and G70 /April on human peripheral T cell proliferation



1994-1995

r-G70

Fig. 7

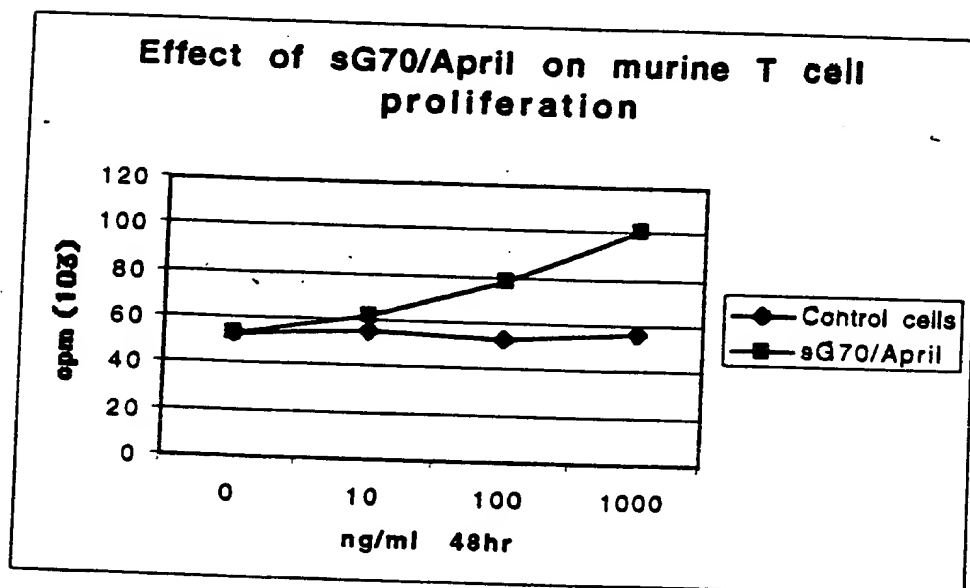
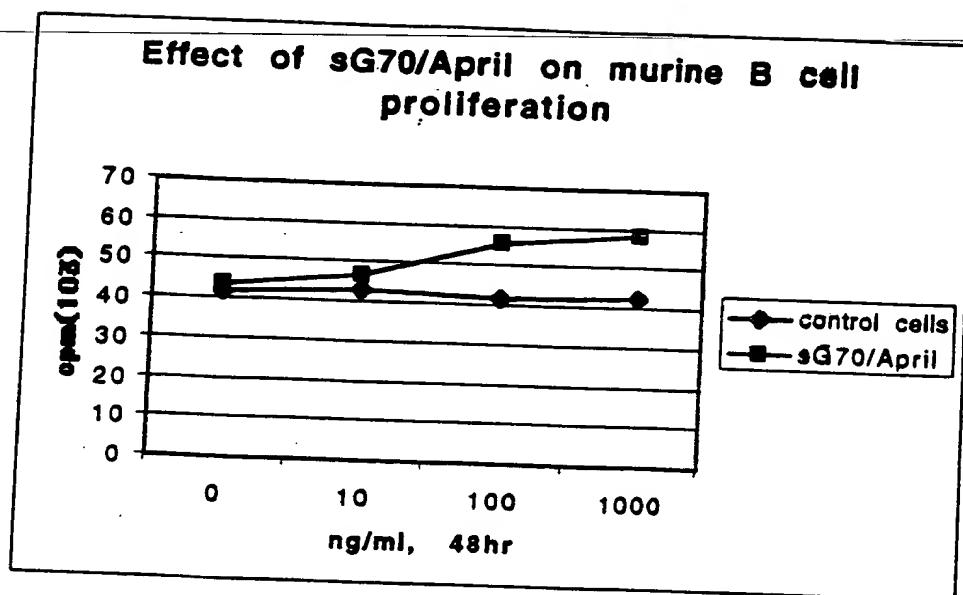


Fig. 8

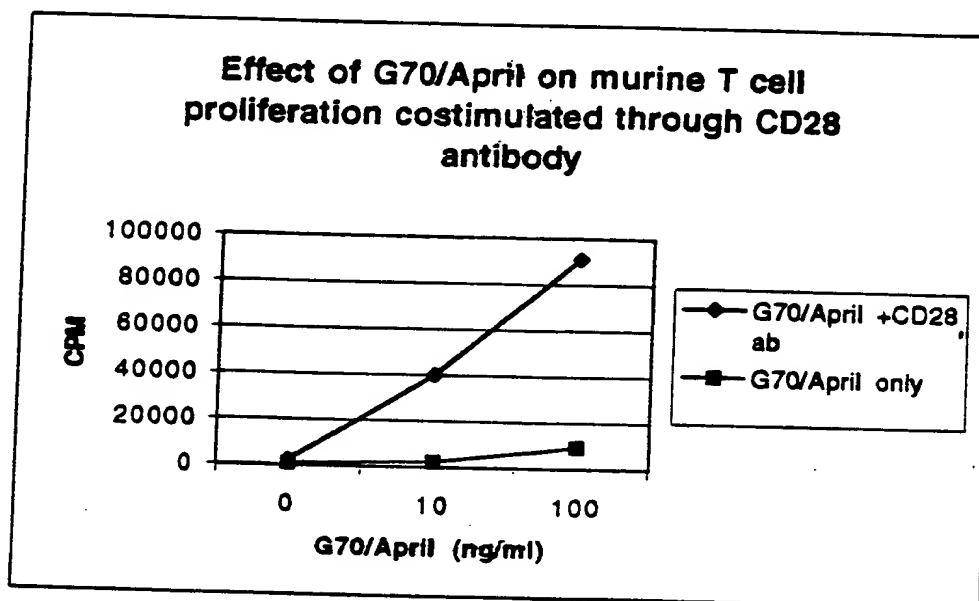


Fig. 9

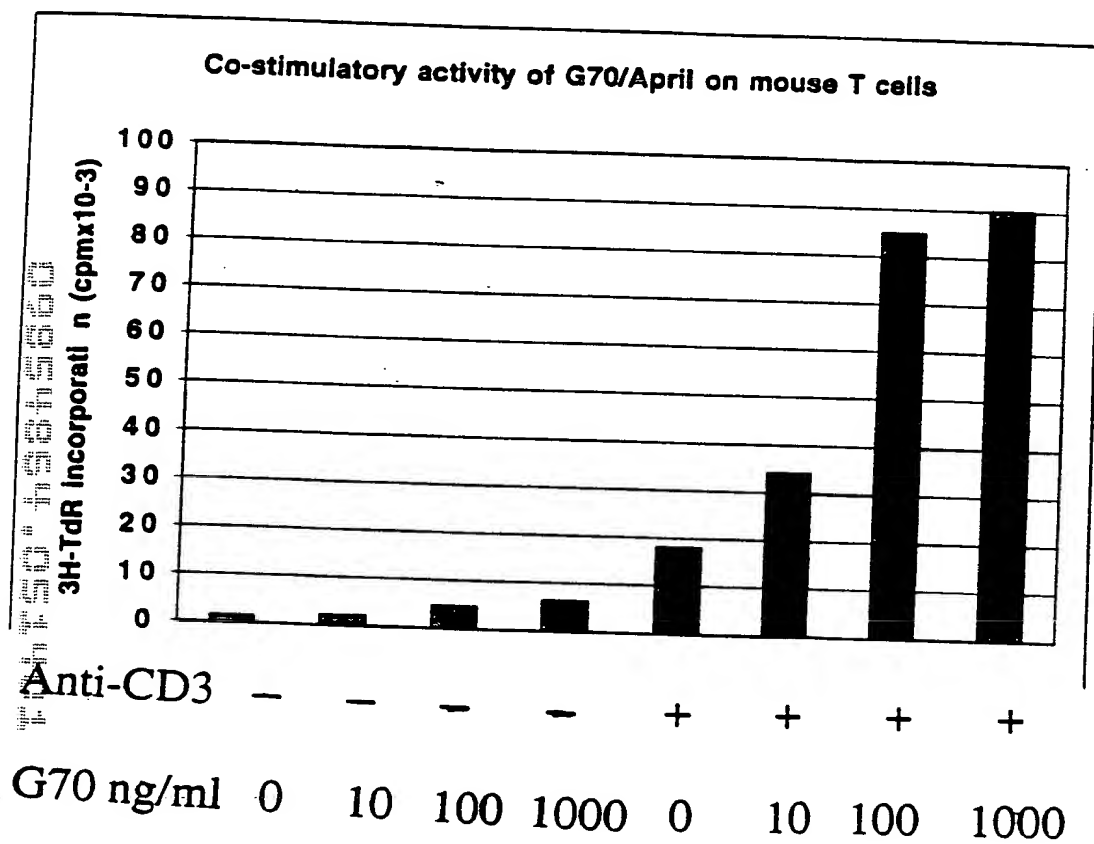


Figure 10A
Human BCMA

Human (SEQ ID NO: 5):

1 MAGQCSQNEY FDSLLHACIP CQLRCSSNTP PLTCQRYCNA
SVTNSVKGTN

51 AILWTCLGLS LIISLAVFVL MFLLRKISSE PLKDEFKNTG
SGLLGMANID

101 LEKSRTGDEI ILPRGLETV EECTCEDCIK SKPKVDS DHC
FPLPAMEEGA

151 TILVTTKTND YCKSLPAALS ATEIEKSISA R

Human (SEQ ID NO: 5):

MAGQCSQ NEYFDSLLHA CIPCQLRCSS NTPPLTCQRY CNASVTNSVK
GTNA ILWTCL GLSLIISLAV FVLMFLLRKI SSEPLKDEFK NTGSGLLGMA
NIDLEKSRTG DEILPRGLE YTVEECTCED CIKSKPKVDS DHC FPLPAME
EGATILVTTK TNDYCKSLPA ALSATEIEKS ISAR

hBCMA's extracellular domain (SEQ ID NO: 6):

MAGQCSQ NEYFDSLLHA CIPCQLRCSS NTPPLTCQRY CNASVTNSVK
GTNA

hBCMA's cysteine-rich consensus region (SEQ ID NO: 7):

CSQ NEYFDSLLHA CIPCQLRCSS NTPPLTCQRY C

hBCMA's transmembrane region (SEQ ID NO: 8):

ILWTCL GLSLIISLAV FVLMF

Figure 10B

huBCMA-Fc (SEQ ID NO: 9):

MAGQCSQNEYFDSLLHACIPCQLRCSSNTPPLTCQRYCNASVTNSVKGTNA
GGGGGDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDV
SHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG
KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCL
VKGFYPSDIAVEWESNGQPENNYKTTPVLDSGDSFFLYSKLTVDKSRWQQ
GNVFSCSVMHEALHNHYTQKSLSLSPGK*

muBCMA-Fc (SEQ ID NO: 10):

MAQQCFHSEYFDSLLHACKPCHLRCSNPPATCQPYCDPSVTSSVKGSYTG
GGGGDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS
HEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGK
EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLV
KGFYPSDIAVEWESNGQPENNYKTTPVLDSGDSFFLYSKLTVDKSRWQQ
GNVFSCSVMHEALHNHYTQKSLSLSPGK*

[illegible]

```

1  MAQQCFHSEY FDSLHACKP CHLRCSNPPA TCQPYCDPSV TSSVKGTYTV
51 LWIFLGLTLV LSLALFTISF LLRKMNPEAL KDEPQSPGQL DGSAQLDKAD
101 TELTRIRAGD DRIFPRSLEY TVEECTCEDC VKSKPKGDS D HFFPLPAMEE
151 GATILVTTKT GDYGKSSVPT ALQSVGMMEK PTHTR

```

```

Query:      4  MAGQCSQMEYFDSLLEHACIPQLCRSSNTFPLTCQRYCNASVTNSVKGTNAILWTCLGLS 63
           MA QC  +EYFDSLLEHAC PC LRCS+  PP TCQ YC+ SVT+SVKGT +LW LGL+
Sbjct:      1  MAQQCFHSEYFDSLLEHACKPCHLRCSN--PPATCQPYCDPSVTSSVKGYTYTLWIFLGLT 58

Query:     64  LIISLAVFVLMFLLRKISSEPLKDEFKNTG----SGLLGMANIDLEKSRTGDEIILPRGL 119
           L++SLA+F + FLLRK++ E LKDE ++ G   S  L  A+ +L + R GD+ I PR L
Sbjct:     59  LVLSLALFTISFLLRKMNPEALKDEPQSPGQLDGSAQLDKADTELTRIRAGDDRIFPRSL 118

Query:    120  EYTVEECTCEDCIKSKPKVSDSDHCFPLPAMEEGATILVTTKTNDYCKS-LPAAL-SATEI 177
           EYTVEECTCEDC+KSKPK DSDH FPLPAMEEGATILVTTKT DY KS +P AL S   +
Sbjct:    119  EYTVEECTCEDCVKSKPKGSDSDHFFPLPAMEEGATILVTTKTGDYGKSSVPTALQSVMGM 178

Query:    178  EKSISAR 184
           EK      R
Sbjct:    179  EKPTHTR 185

```

Figure 12A
Human TACI

huTACI (SEQ ID NO: 14).

1 MSGLGRSRRG GRSRVDQEER FPQGLWTGVA MRSCPEEQYW DPLLGTCTMSC
51 KTICNHQSQR TCAAFCRSLS CRKEQGKFYD HLLRDCISCA SICGQHPKQC
101 AYFCENKLRS PVNLPPELRR QRSGEVENNS DNSGRYQGLE HRGSEASPAL
151 PGLKLSADQV ALVYSTLGLC LCAVLCCFLV AVACFLKKRG DPCSCQPRSR
201 PRQSPAKSSQ DHAMEAGSPV STSPEPVETC SFCFPECRAP TQESAVTPGT
251 PDPTCAGRWG CHTRTTVLQP CPHIPDSGLG IVCVPAQEGG PGA

MSGLGRSRRGGRSRVDQEERFPQGLWTGVAMRSCPEEQYWDPLLGTCTMSC
KTICNHQSQRRTCAAFCRSLSRKEQGKFYDHLLRDCISCASICGQHPKQC
AYFCENKLRS PVNLPPELRRQRSGEVENNSDNSGRYQGLEHRGSEASPAL
PGLKLSADQVALVYSTLGLCLCAVLCCFLVAVACFLKKRGDPCSCQPRSR
PRQSPAKSSQDHAMEAGSPVSTSPEPVETCSFCFPECRAPTQESAVTPGT
PDPTCAGRWGCHTRTTVLQPCPHIPDSGLGIVCVPAQEGGPGA

huTACI's extracellular domain (SEQ ID NO: 15):

1 MSGLGRSRRG GRSRVDQEER FPQGLWTGVA MRSCPEEQYW DPLLGTCTMSC
51 KTICNHQSQR TCAAFCRSLS CRKEQGKFYD HLLRDCISCA SICGQHPKQC
101 AYFCENKLRS PVNLPPELRR QRSGEVENNS DNSGRYQGLE HRGSEASPAL
151 PGLKLSADQV ALVYST

Figure 12B

huTACI's cysteine-rich consensus region (SEQ ID NO: 16):

CPEEQYWDPLLGTCTMCKTICNHQSQRTCAAFC and

CRKEQGKFYDHLLRDCISCASICGQHFKQCAAYFC

transmembrane region (SEQ ID NO: 17):

LGLCLCAVLCCFLVAVACFL

hTACI-Fc (SEQ ID NO: 18):

1 MSGLGRSRRG GRSRVDQEEF FPQGLWTGVA MRSCPEEQYW DPLLGTCTMSC
51 KTICNHQSQRTCAAFCRSLS CRKEQGKFYD HLLRDCISCA SICGQHFKQC
101 AYFCENKLS PVNLPPELRR QRSGEVENNS DNSGRYQGLE HRGSEASPAL
151 PGLKLSADQV ALVYSGGGGG DKTHTCPPCP APELLGGPSV FLFPPKPKDT
201 LMISRTPEVT CVVVDVSHED PEVKFNWYVD GVEVHNAKTK PREEQYNSTY
251 RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK GQPREPQVYT
301 LPPSRDELTK NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTTPVLDS
351 DGSFFLYSKL TVDKSRWQQG NVFSCSVME ALHNHYTQKS LSLSPGK*

Alignment of cysteine rich extracellular regions of human

34 CPEEQYWDPLLGTCMSCKTICNHQS.QRTCAAFCSRSLSCRKEQGKFYDHL 82
| : : | | | . | . | . | | : | . | :
8 CSQNEYFDSLLHACIPCLRCSNTPPLTCQRYCNASVTNSVKGT..NAI 55

83 LRDCISCASI 92

56 LWTCLGLSLI 65

2010年12月10日

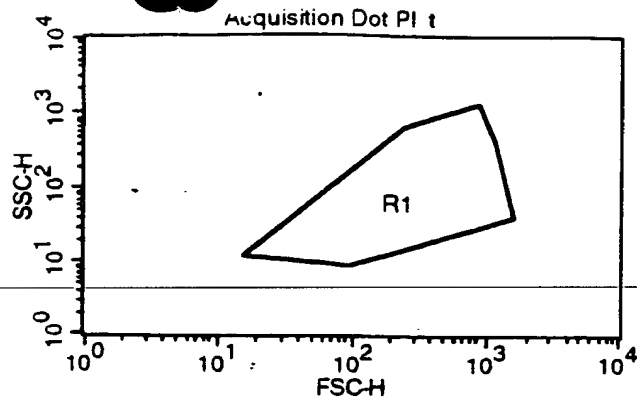
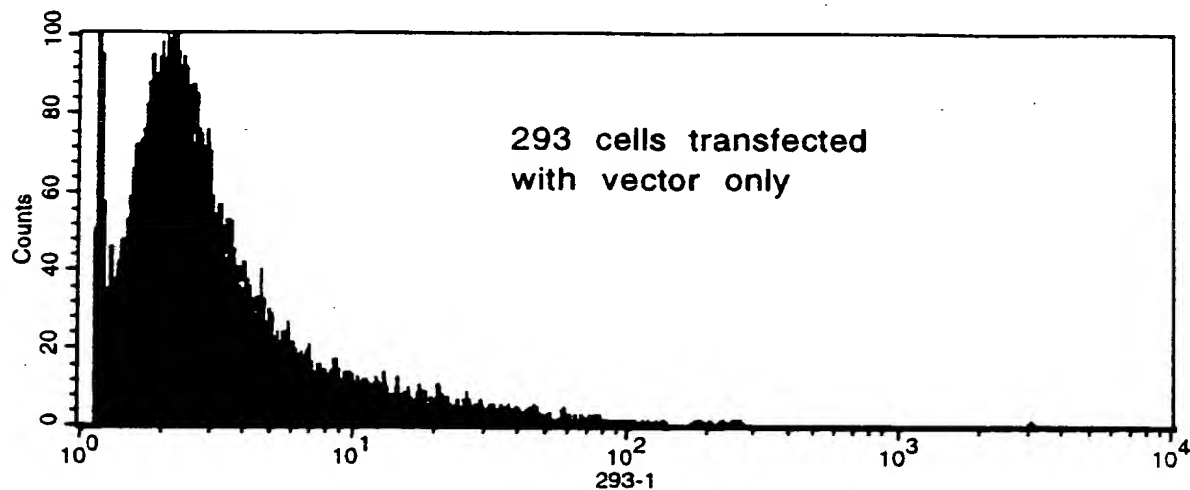
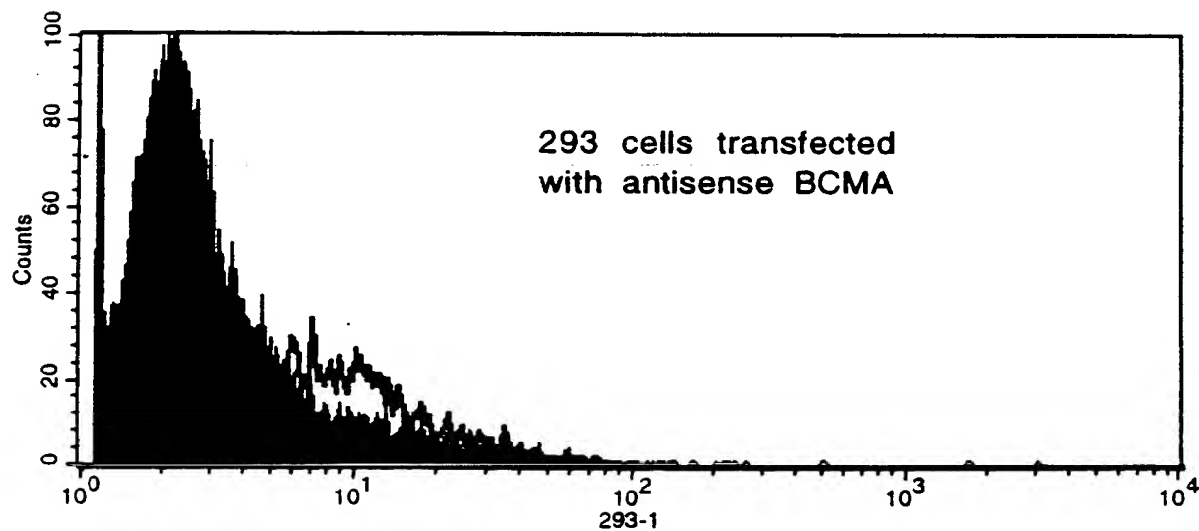


Fig.14



A.



B.

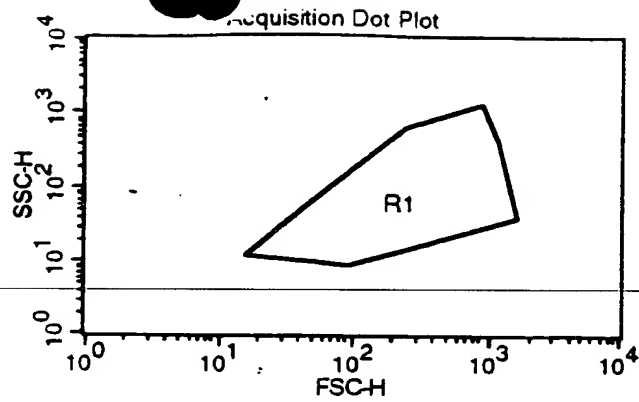
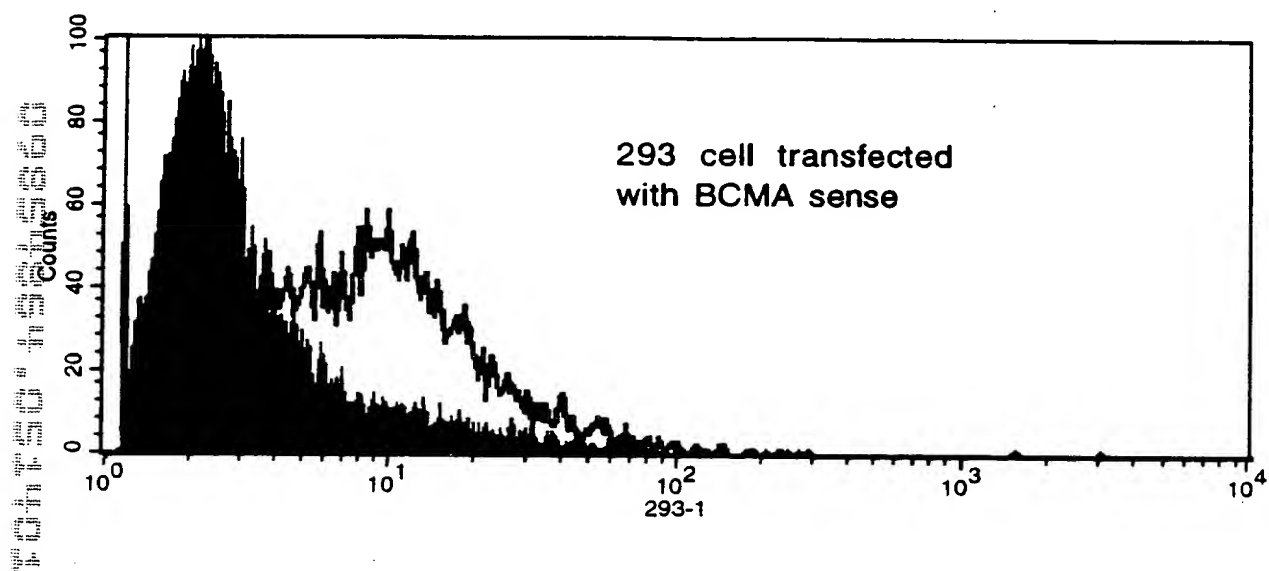


Fig.14



C.

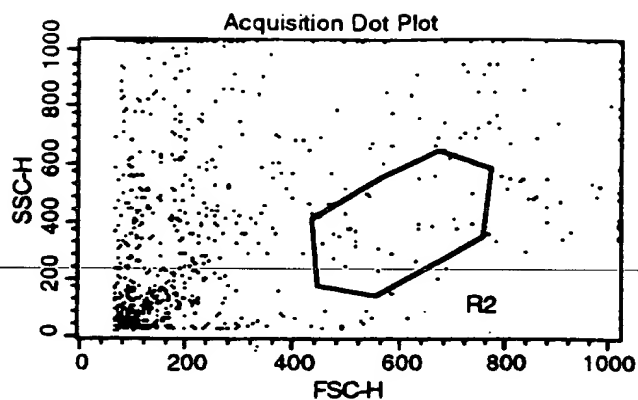
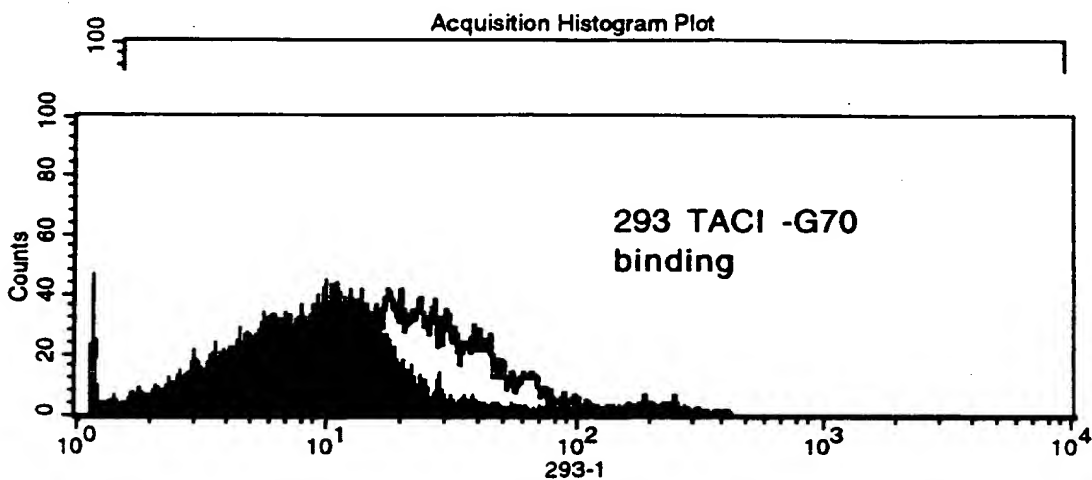
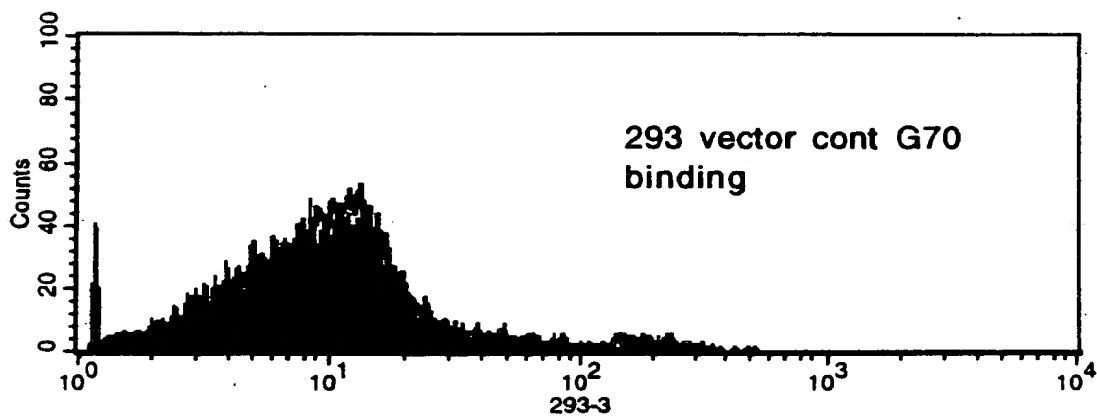


Fig. 15



A.



B.

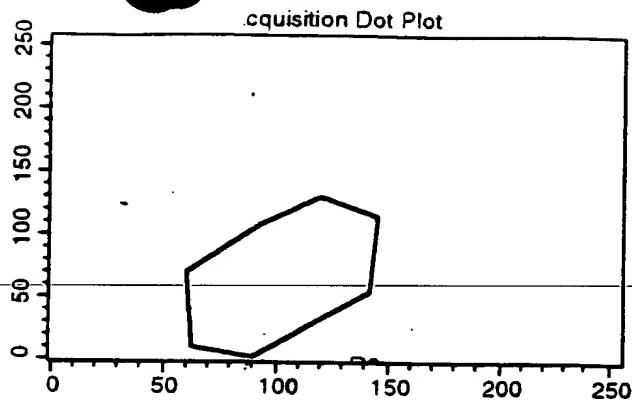
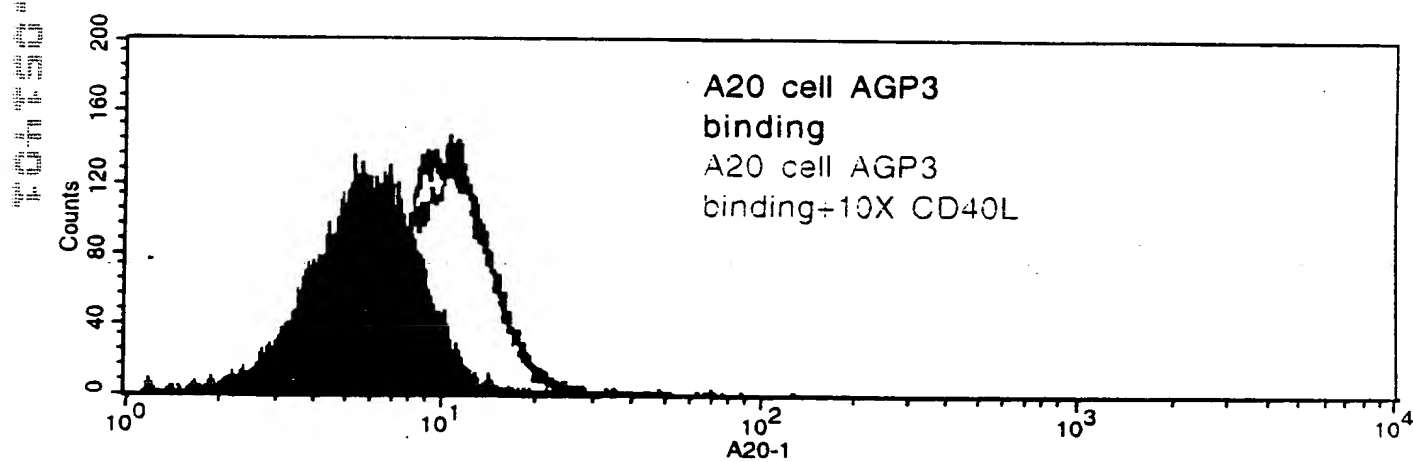
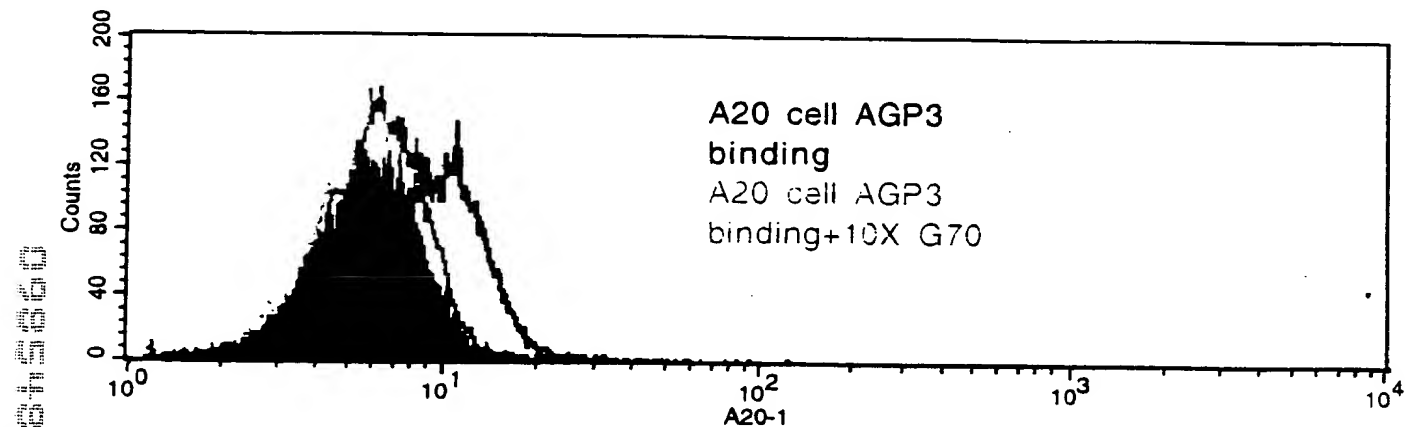


Fig. 16



Experiment 4-3-2000

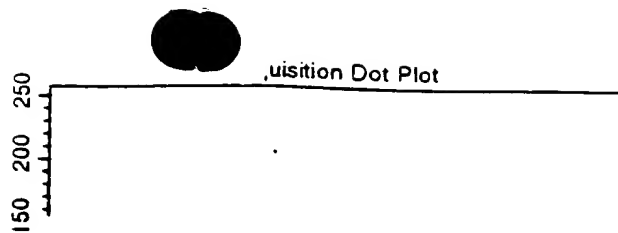
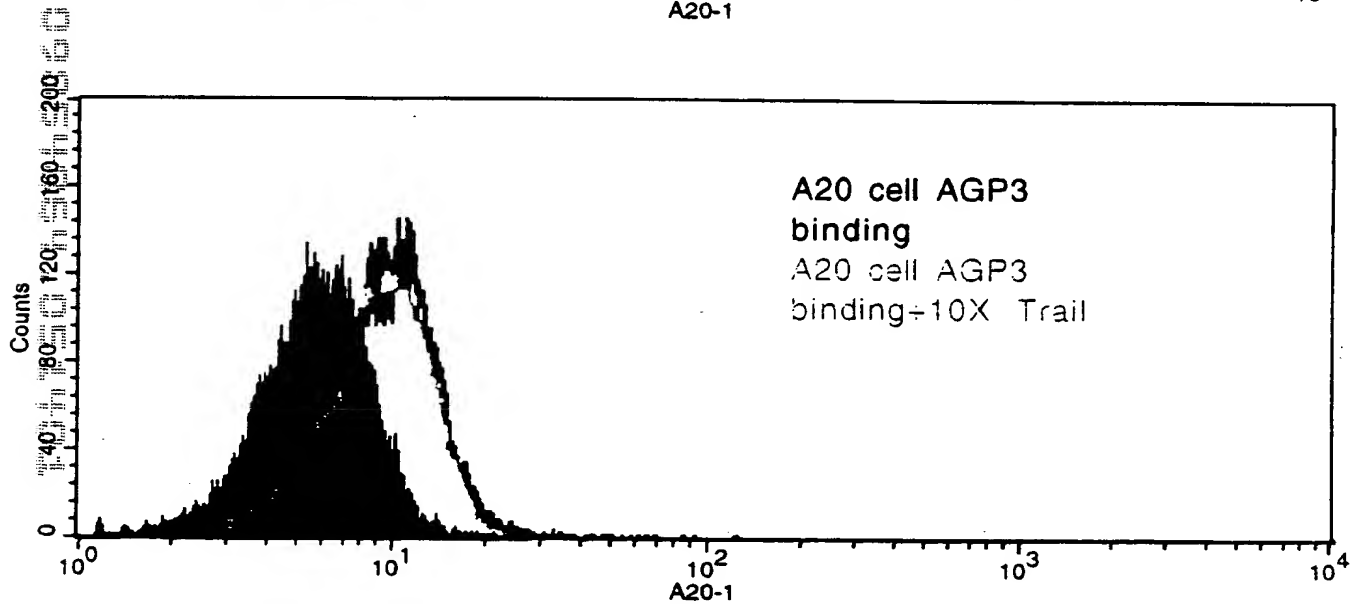
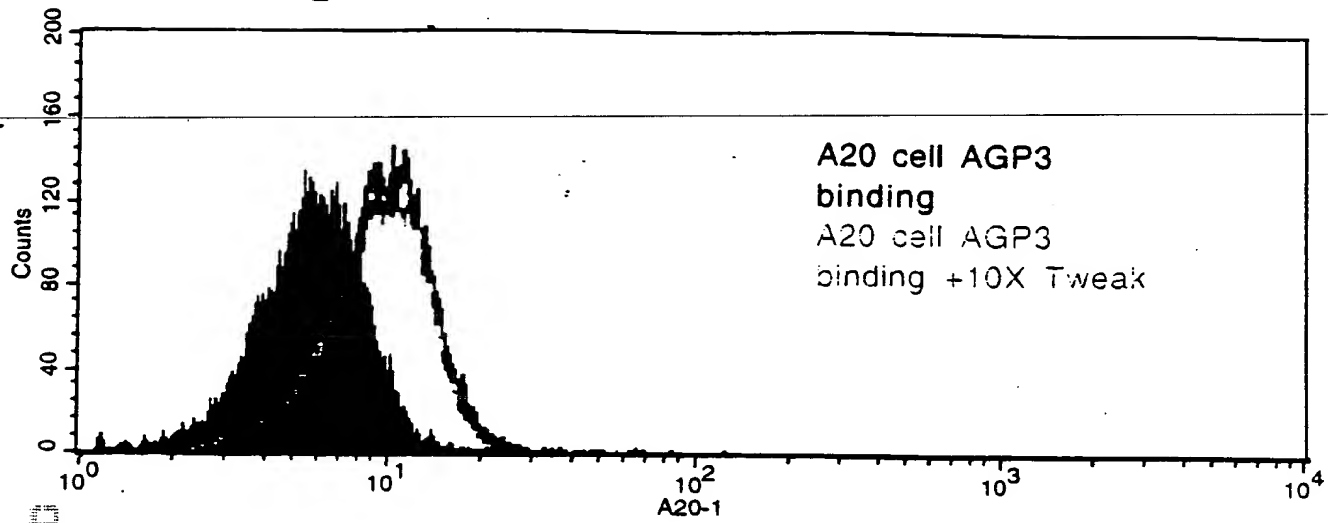


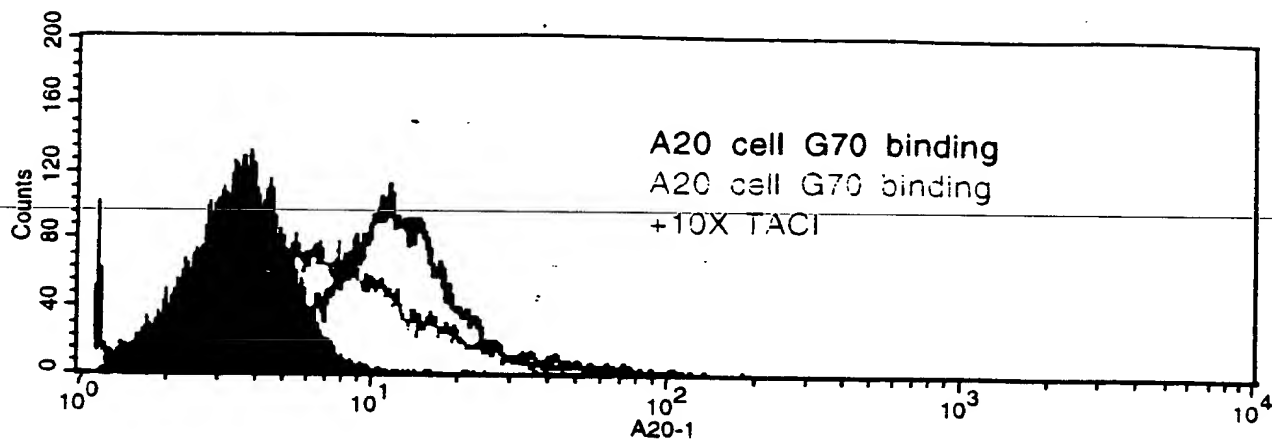
Fig. 16



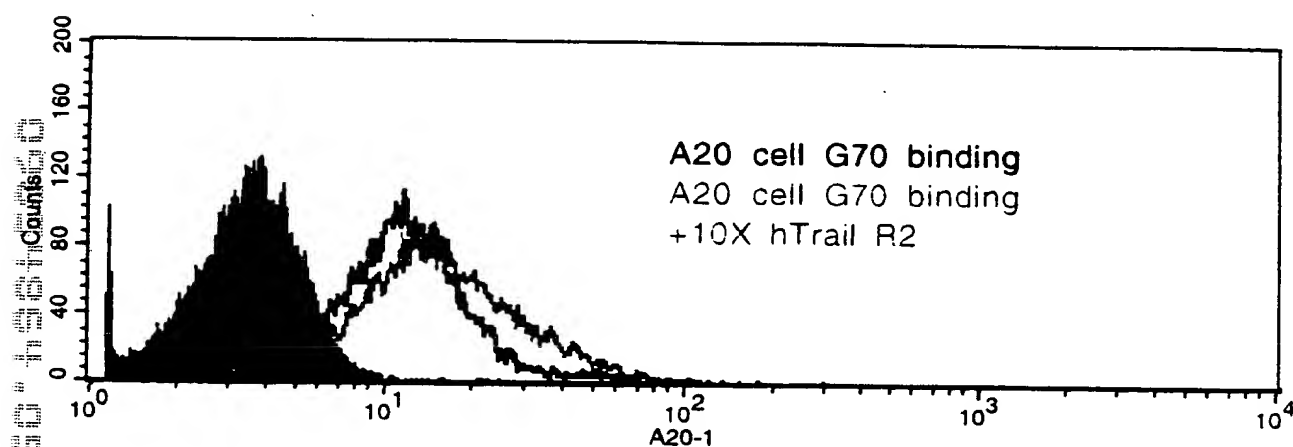
Experiment 4-3-2000

Fig.17

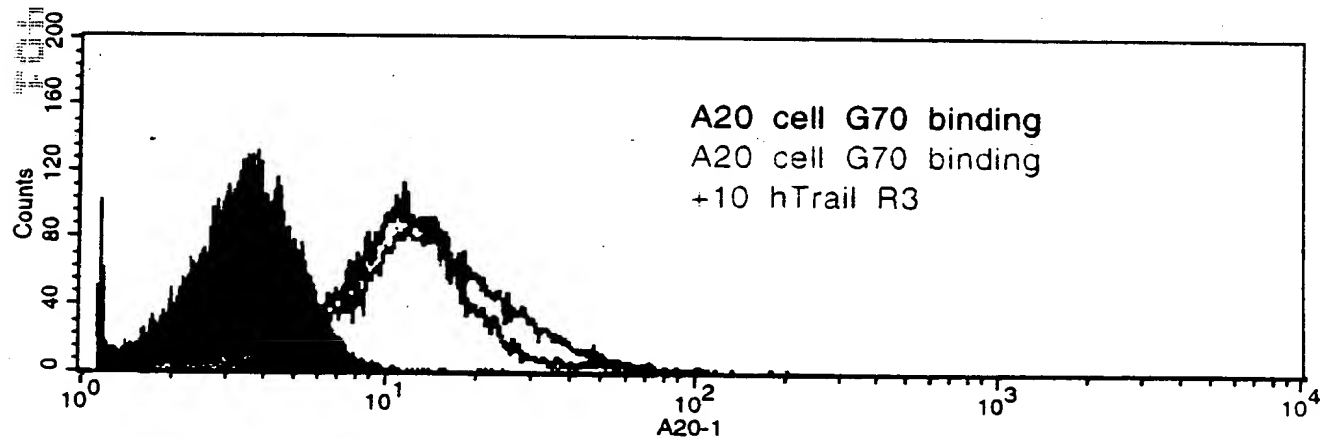
A.



B.



C.



Experiment
4-11-2000

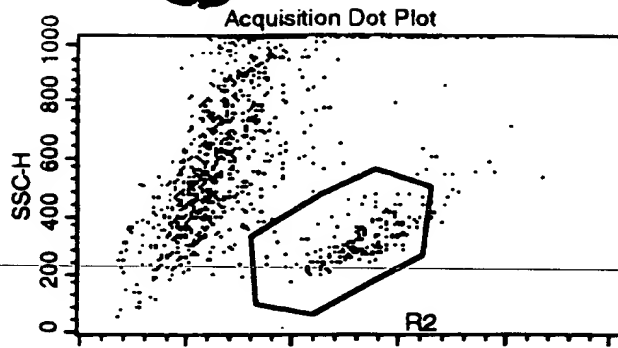
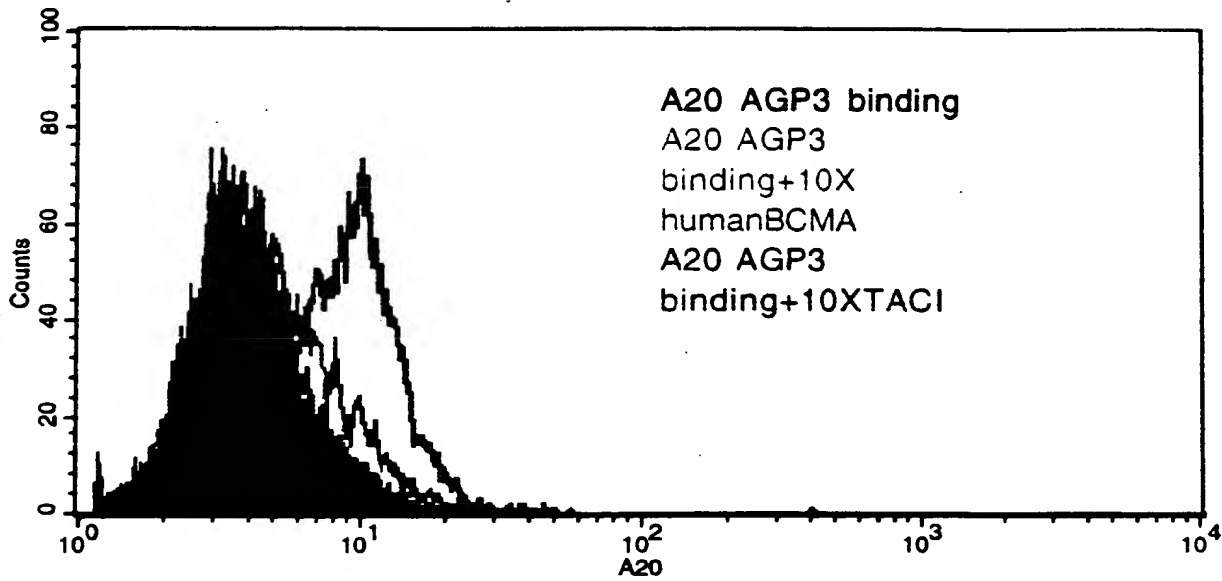


Fig.18



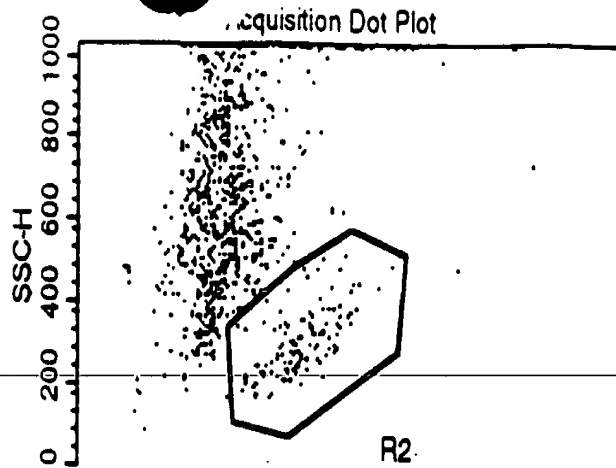


Fig.19

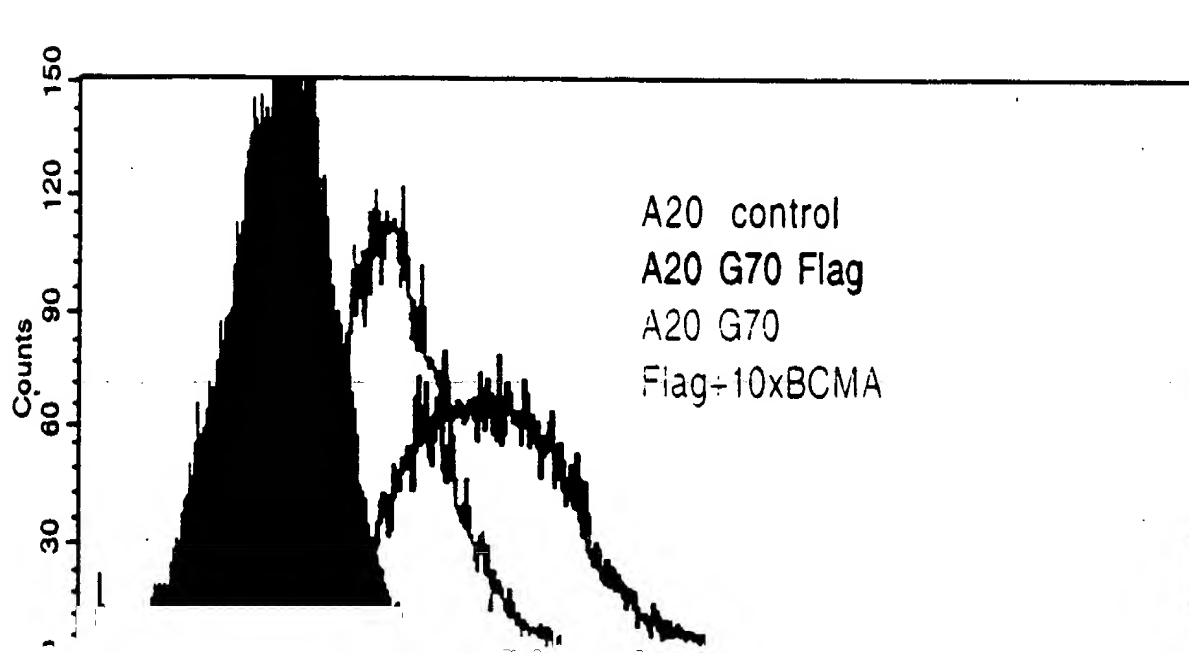
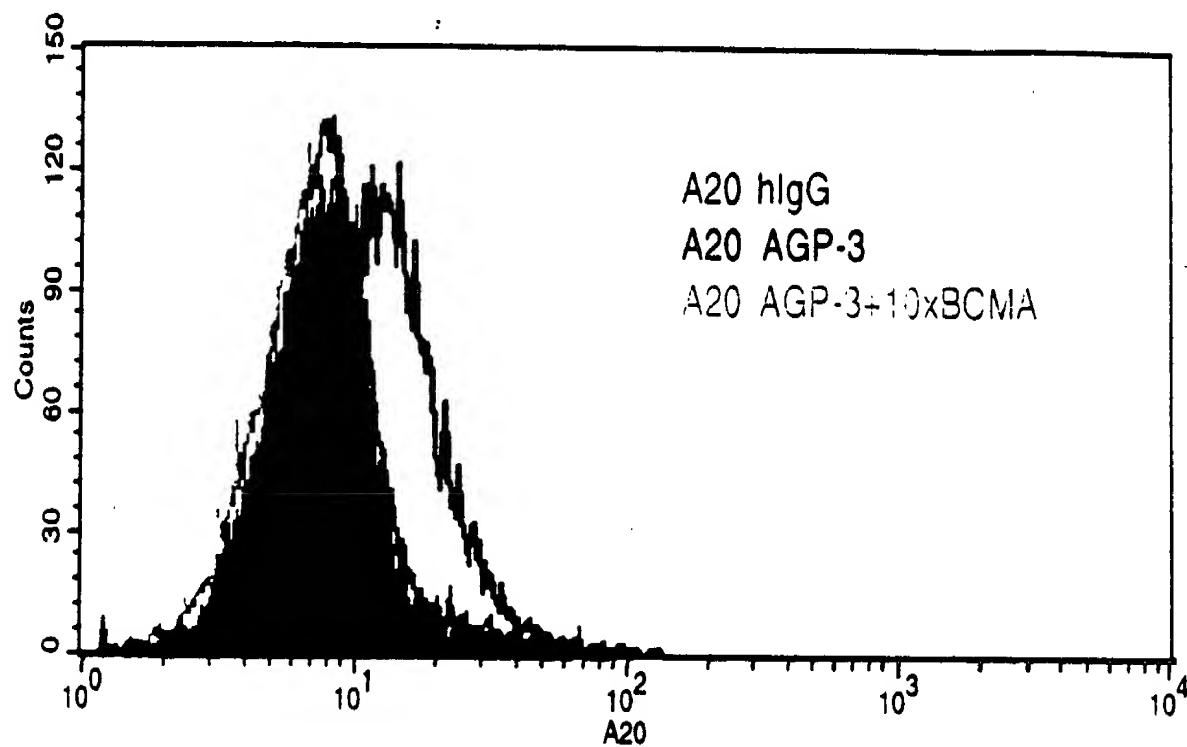


Fig.20

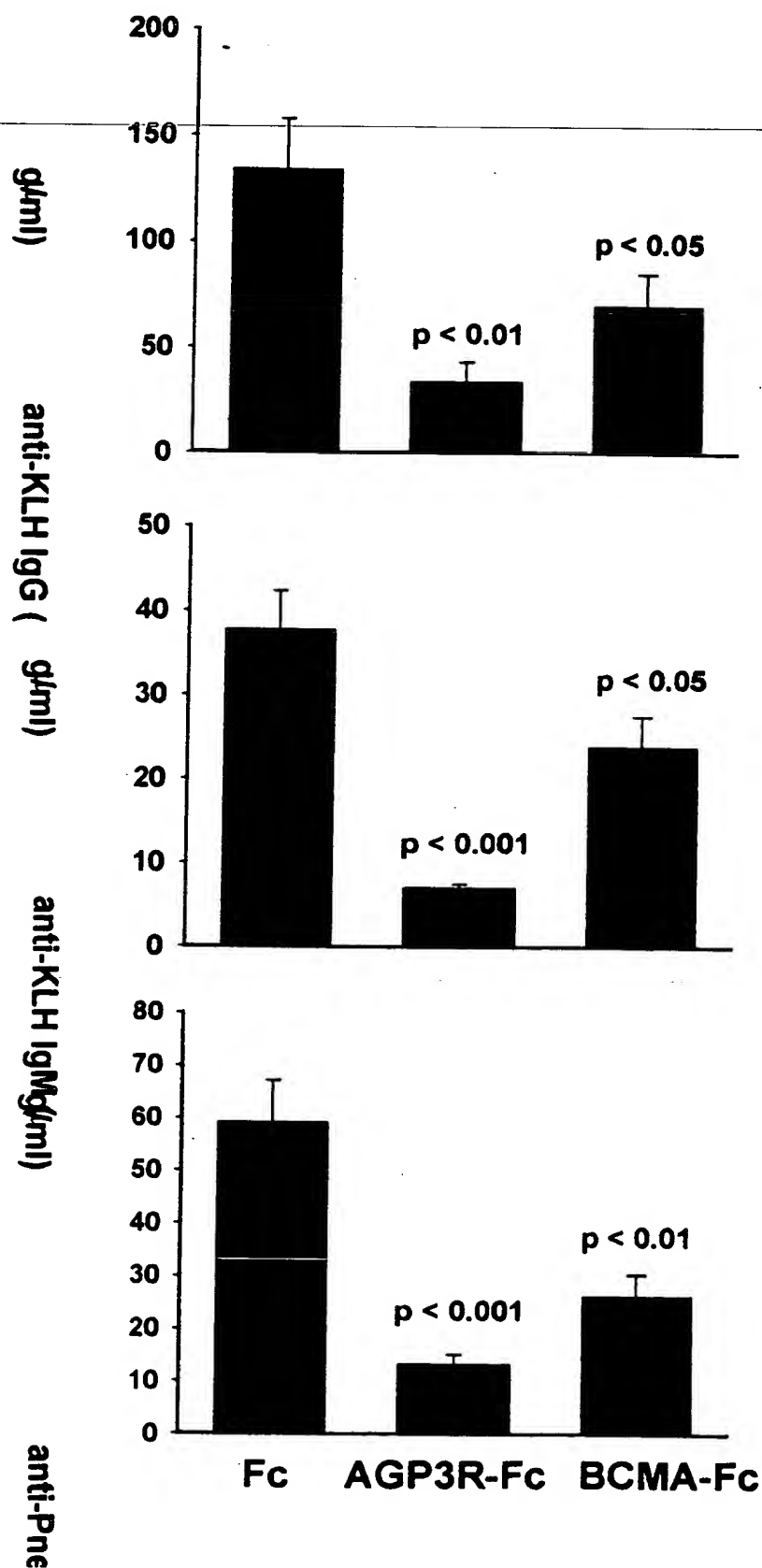


Figure 21 Fc-humanAPRIL

Fc-humanAPRIL protein sequence including the signal sequence, Fc domain, linker (XhoI site) and April:

```

1 MEWSWVFLFF LSVTTGVHSD KTHTCPPCPA PELLGGPSVF
  LPPKPKDRTL
51 MISRTPEVTC VVVDVSHEDP EVKFNWYVDG VEVHNAKTKP
  REEQYNSTYR
101 VVSVLTVLHQ DWLNGKEYKC KVSNKALPAP IEKTISKAKG
  QPREPQVYTL
151 PPSRDELTKN QVSLTCLVKG FYPSDIAVEW ESNGQPENNY
  KTTPPVLDSD
201 GSFFLYSKLT VDKSRWQQGN VFSCSVMHEA LHNHYTQKSL
  SLSPGKSRAV
251 LTQKQKKQHS VLHLVPINAT SKDDSDVTEV MWQPALRRGR
  GLQAQGYGVR
301 IQDAGVYLLY SQVLFQDVTF TMGQVVSREG QGRQETLFRC
  IRSMPSHPDR
351 AYNSCYSAGV FHLHQGDILS VIIPRarakL NLSPHGTF LG
  FVKL*

```

Figure 22

Fc-HumanAPRIL and soluble human AGP3 stimulate proliferation of primary B cells

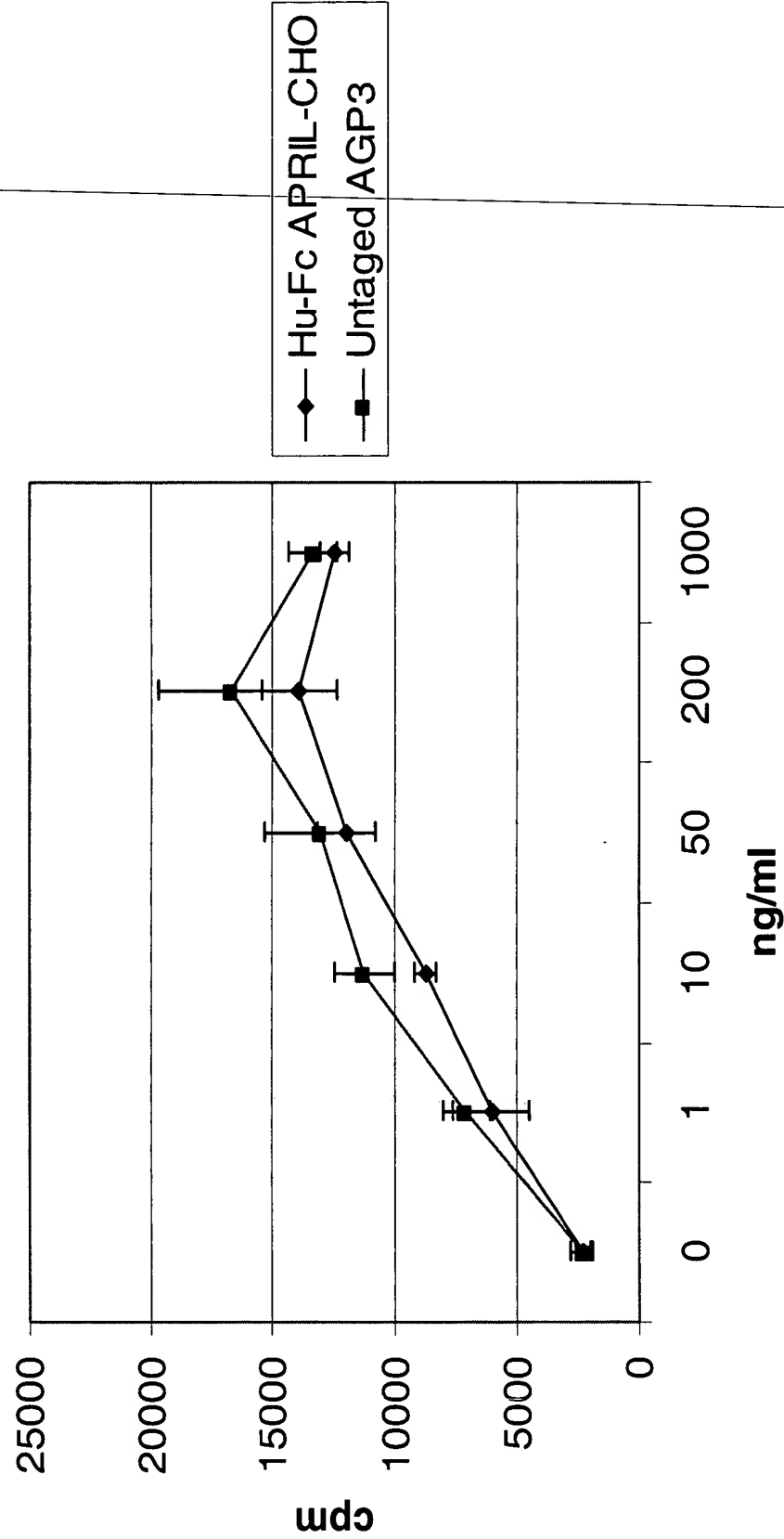


Figure 23

hBCMA-Fc and wt hTACI-Fc inhibits Flag-mAPRIL mediated mouse B cell proliferation

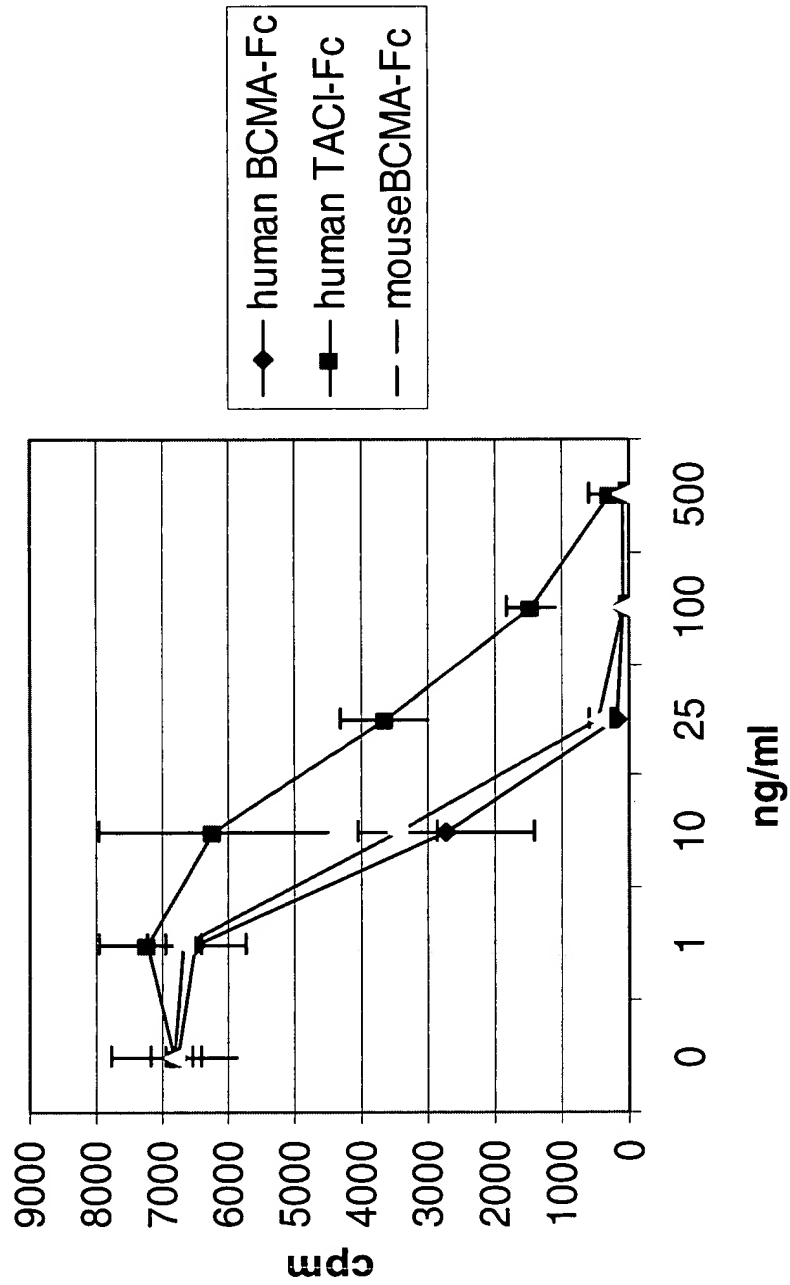


Figure 24:

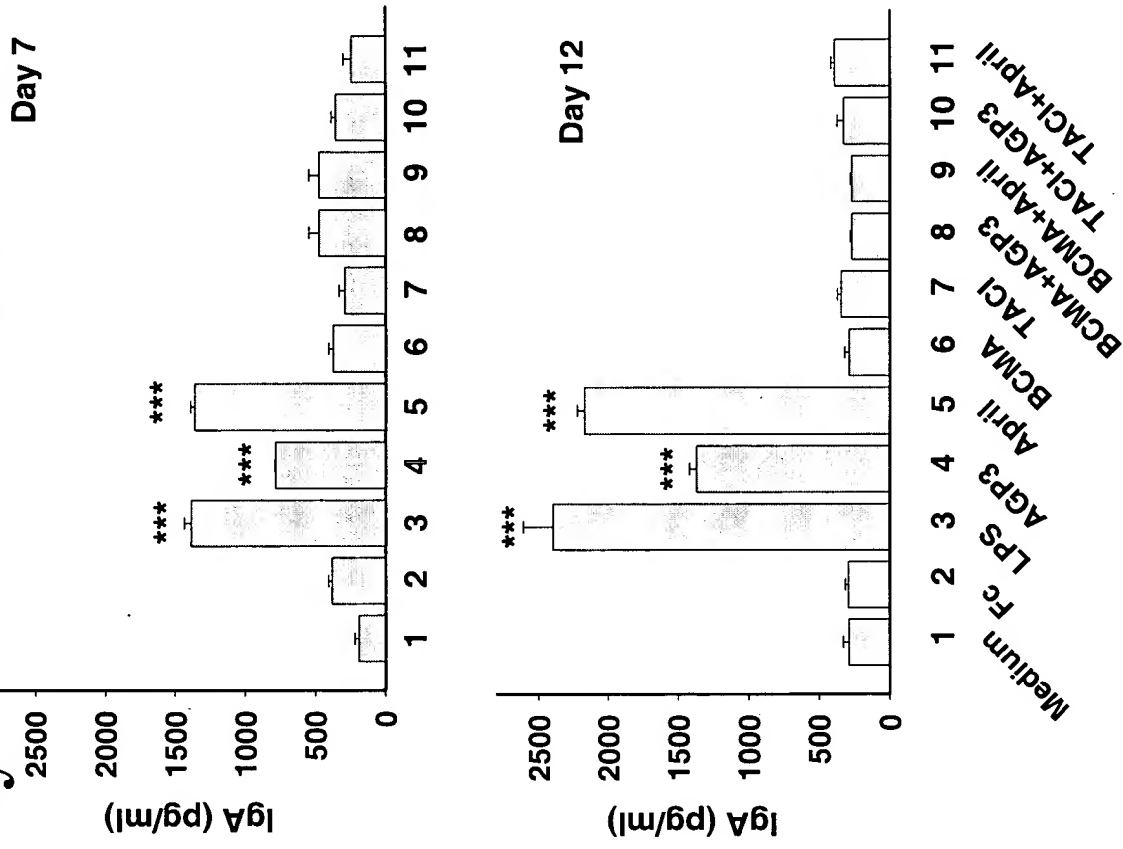
hBCMA-Fc reduces PB B cell level *in vivo*
15 mg/kg ip on day 0, 3, and 6

BLOOD		WBC	#Lym	CD3+	CD3-B220+
		10e6/ml	10e6/ml	#	#
BCMA-Fc		5.30	3.81	2.3	1.3
	SD	0.39	0.43	0.32	0.27
	t test	0.03318	0.01570	0.24737	0.00506
Fc		8.02	6.43	2.7	3.2
	SD	1.27	1.52	0.6	0.6
Saline		6.90	5.55	2.1	2.9
	SD	2.04	1.79	0.5	1.2

spleen	WBC 10e6/ml	Lym (%)	spleen lym# 10ml(x10e6)	CD3-B220+ (%)	CD3-B220+ #
BCMA-Fc	9.12	97.9	89.3	45.5	41.8
SD	0.92	0.51	9.32	1.29	4.92
t test	0.02778	0.89118	0.02668	0.00234	0.02088
Fc	11.49	97.9	112.5	50.6	57.1
SD	1.62	0.38	15.65	1.95	9.67
Saline	11.48	98.5	113.1	53.7	48.5
SD	1.71	0.1	16.9	6.7	29.15

Figure 26

Flag-mAPRIL and hAGP3 mediated IgA production inhibited by hBCMA-Fc and hTACI-Fc *in vitro*



Flag-mAPRIL and hAGP3 Mediated IgG Production Inhibited by BCMA-Fc and TACI-Fc *in Vitro*

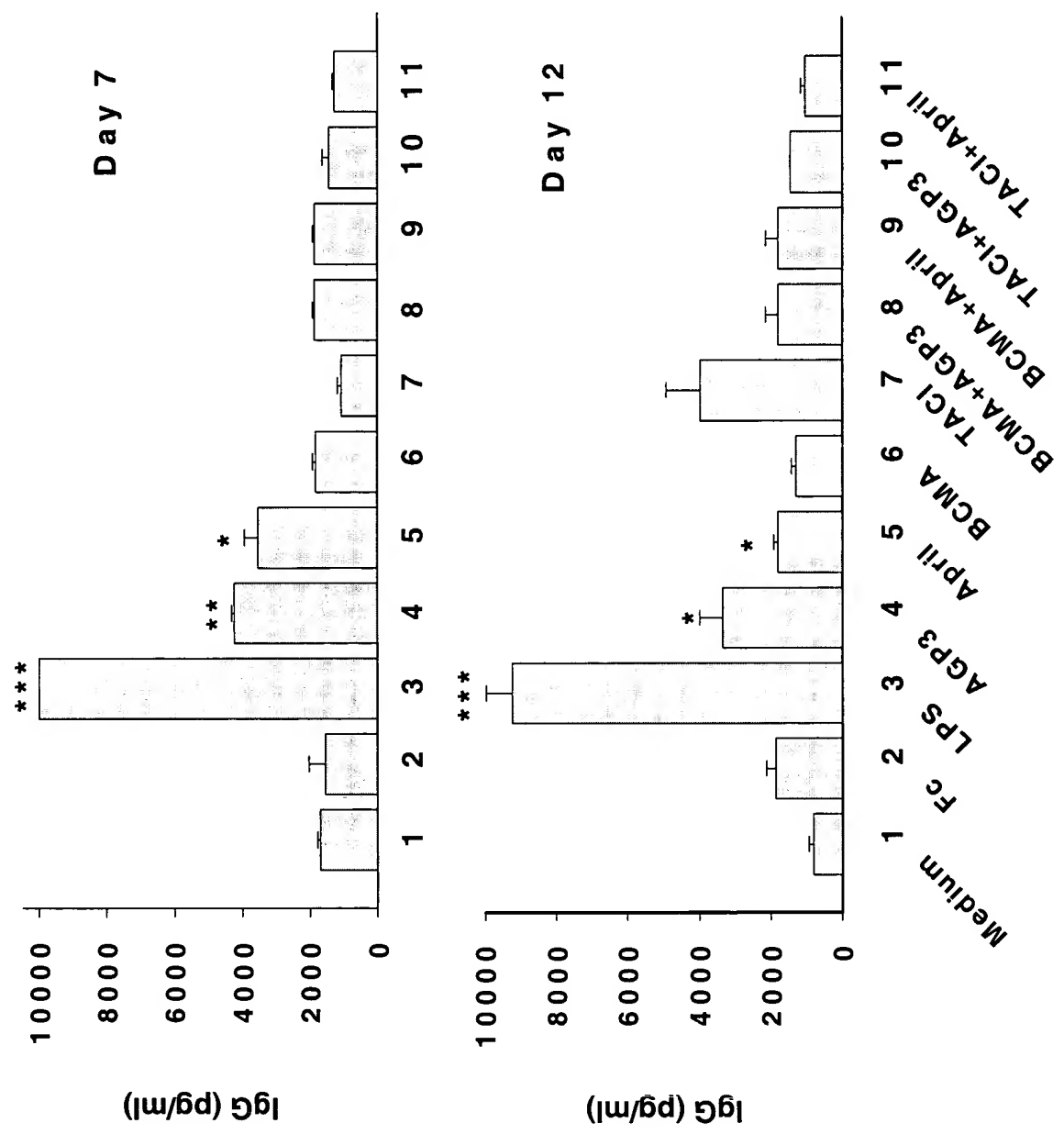


Figure 28: Significantly reduces total IgE and IgA in normal mice treated with mBCMA-Fc and trun hTACI-Fc 5 mg/kg ip day 0, 3, and 6

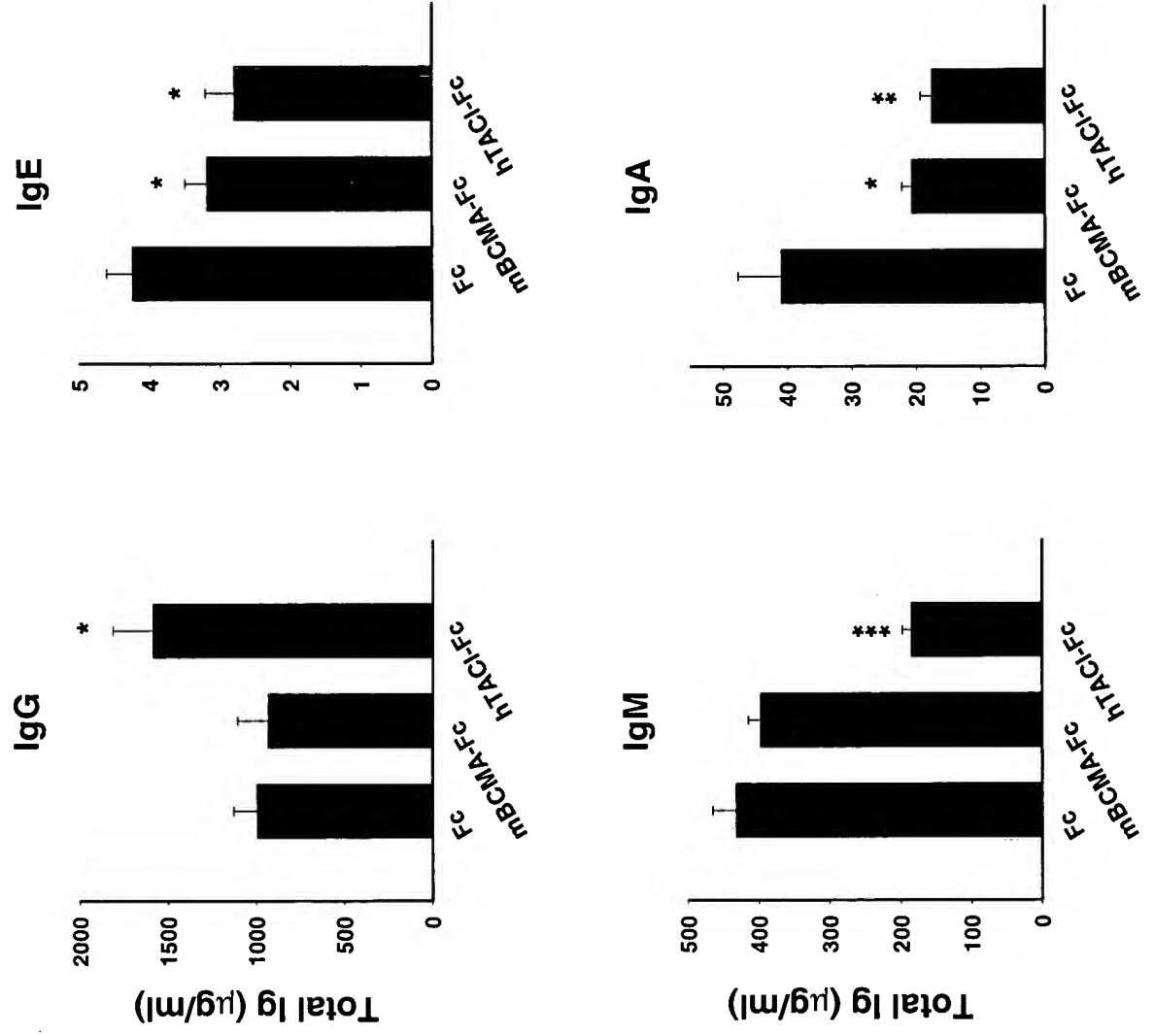
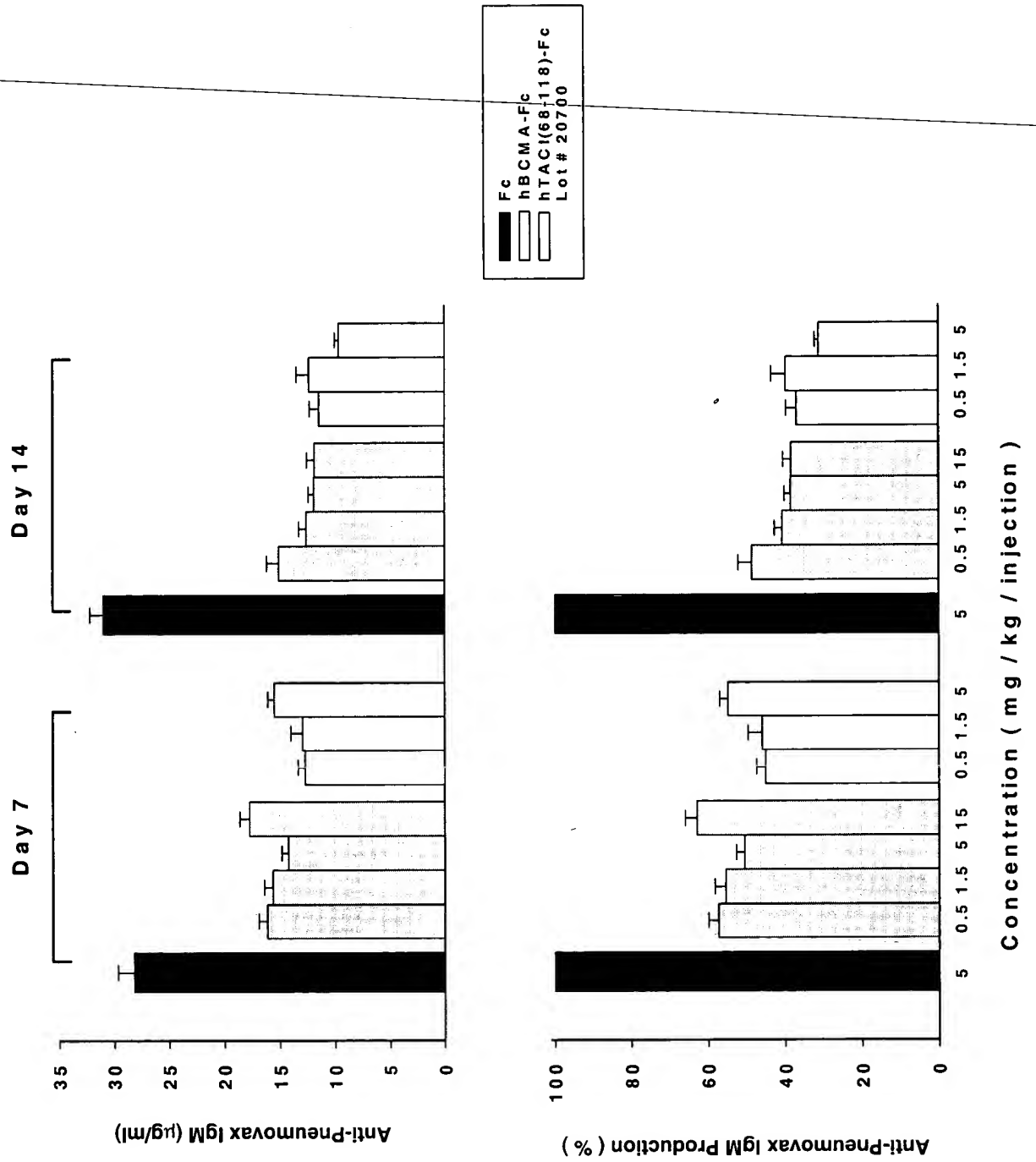


Figure 29: BCMA-Fc and truncated TACI-Fc at daily doses of 0.5 mg/kg inhibits humoral immunity *in vivo*



**Figure 30: Anti-mAPRIL c-19 MAb
inhibition of APRIL mediated B cell
proliferation**

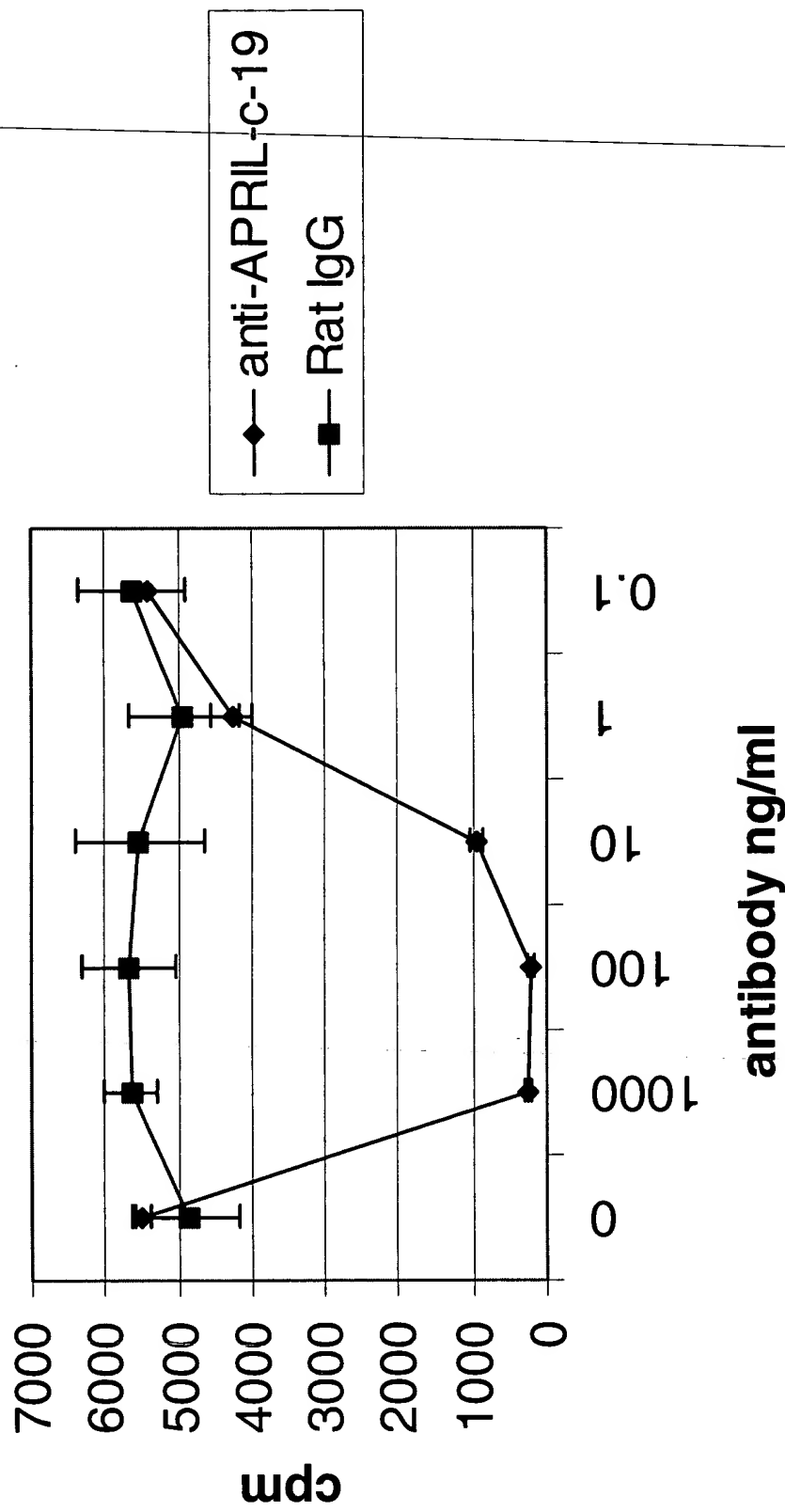
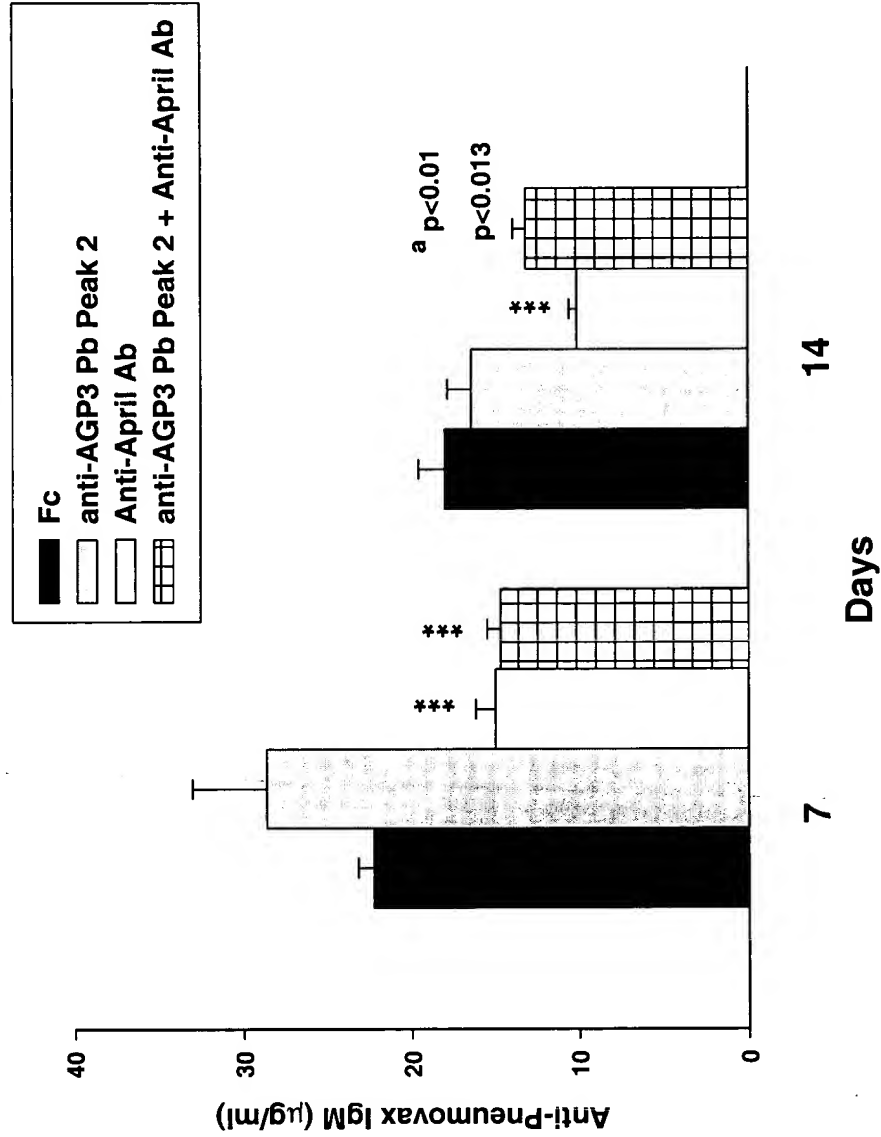


Figure 31

Neutralizing anti-mAPRIL Mab Reduces anti-Pneumovacs IgM *In Vivo*
5 mg/kg ip on day 0, 3, and 6

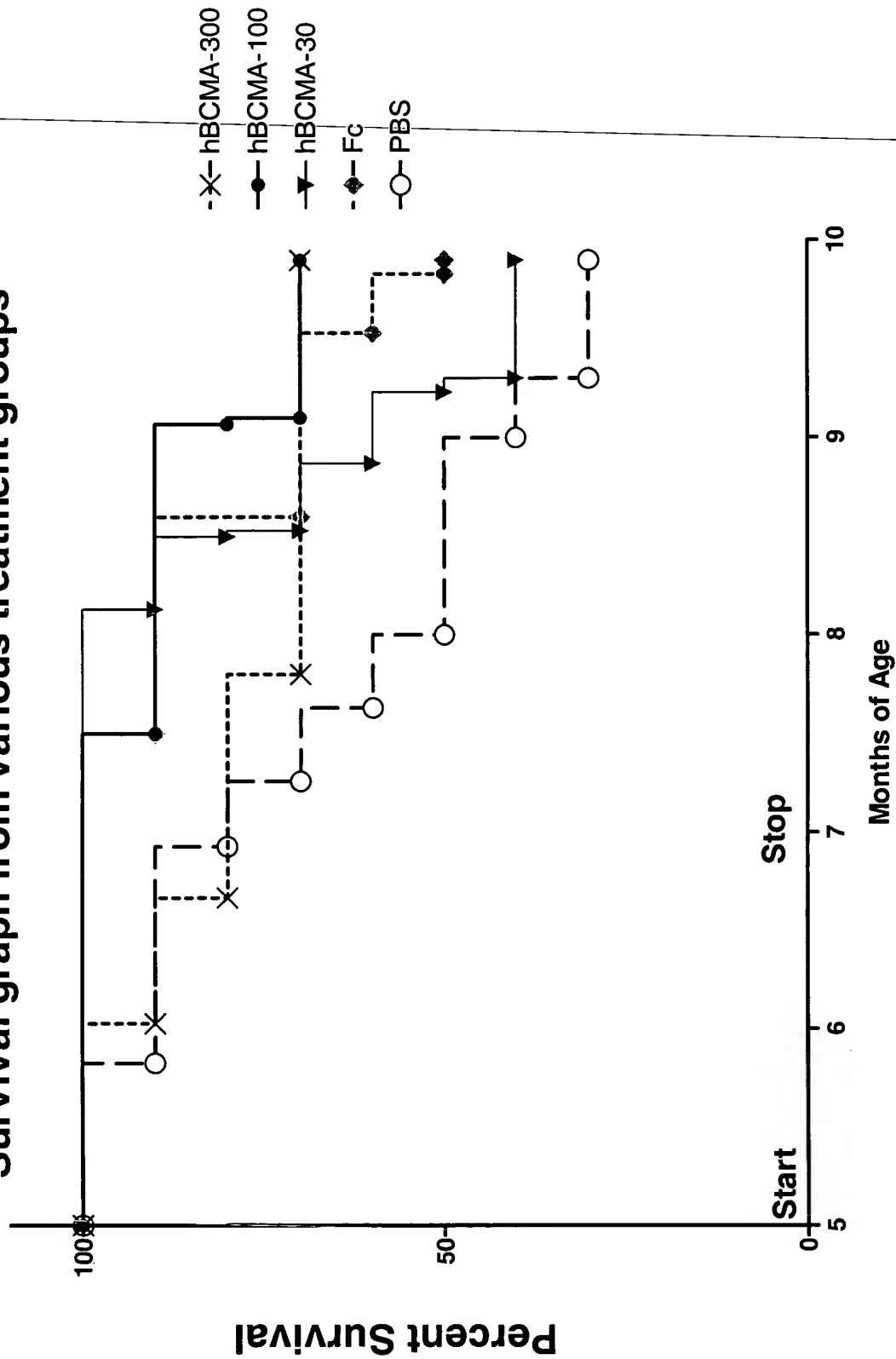


^a difference between Anti-April Ab and anti-AGP3 Pb Peak 2+ Anti-April Ab Groups

12.15.00 lupus xp.

Figure 32: Effect of hBCMA-Fc in NCB/NCWF1 mice

Survival graph from various treatment groups

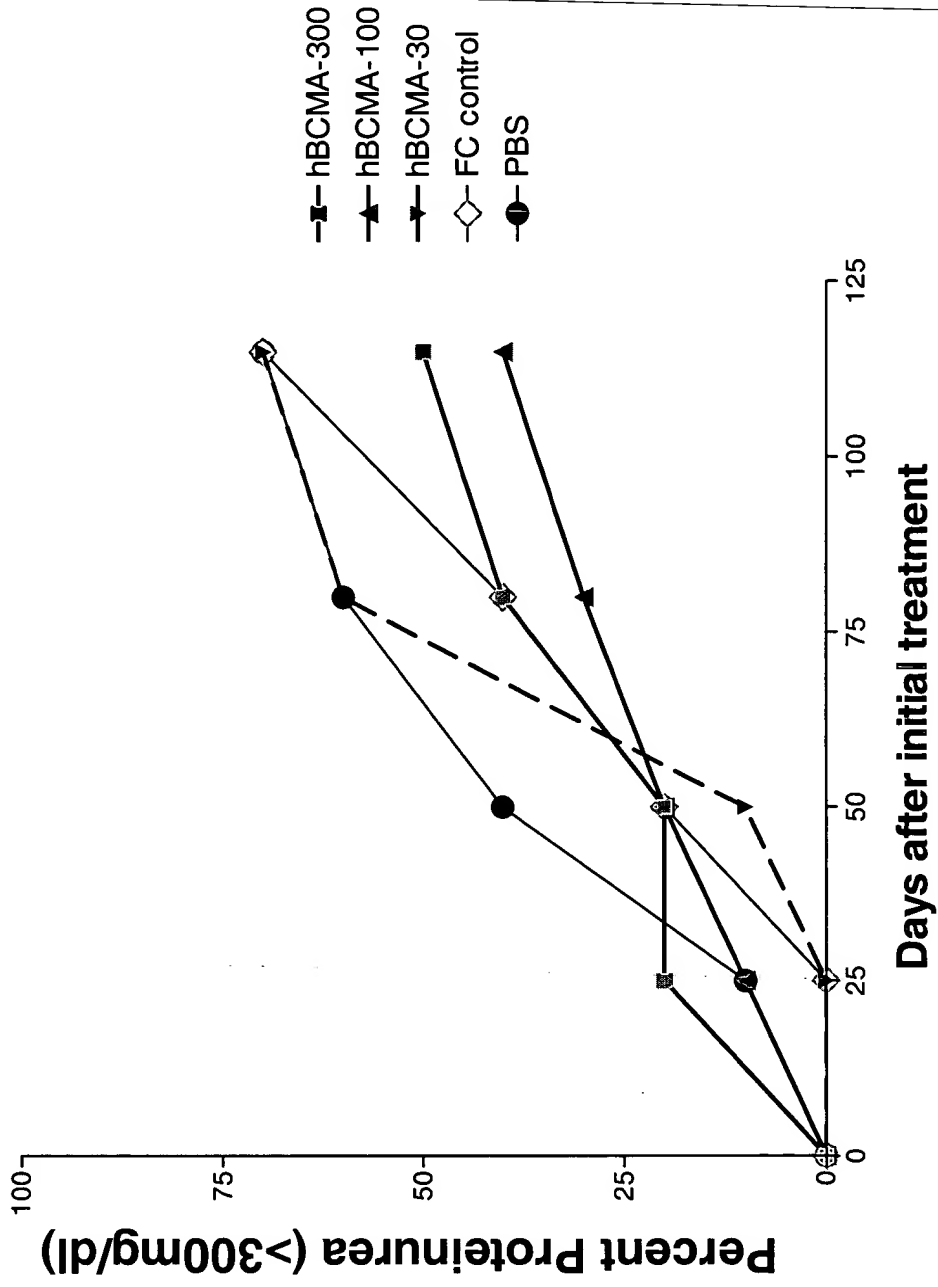


N=10 Mice were treated for 8 weeks 3x/week with the indicated proteins. KIN2 group had 12 mice. The 100 in the legend stands for 100 µg of protein or 4mg/kg i.p.

12.15.00 lupus xp

Figure 33: Effect of hBCMA-Fc in NCB/NCWF1 mice

**Percentage of mice with proteinurea (>300mg/dl)
from various treatment groups**



N=10 Five month old BWf1 mice were treated with protein for 8 weeks i.p.
The hBCMA-300 stands for hBCMA-fc 300µg/mouse (12mg/kg)

Figure 34: Analysis of antibodies to dsDNA from the peripheral blood from various treatment groups of BWF1 at day 0,30,60, and 90.

MEAN anti-dsDNA isotypes in U/ml									
Group #	Day 0		Day 30		Day 60		Day 90		IgM
	IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM	
hBCMA-300	179	560	163	371	150	706	171	841	
hBCMA-100	150	430	259	718	171	822	339	1031	
hBCMA-30	377	592	297	458	401	664	424	601	
FC.	149	371	234	283	384	331	432	351	
PBS	308	292	439	311	247	576	720	467	
Standard Deviation of the above means									
Group #	Day 0		Day 30		Day 60		Day 90		IgM
	IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM	
hBCMA-300	104	303	116	211	62	518	62	734	
hBCMA-100	109	262	306	461	212	758	371	1225	
hBCMA-30	363	455	281	430	305	606	421	400	
FC.	68	160	150	93	391	151	233	237	
PBS	311	73	474	152	247	370	870	327	

Figure 35: Evaluation of B cell numbers at treatment day 60 from the 12mg/kg (30 ug), 4mg/kg (100ug), and 1.3mg/kg (300 ug) dose of hBCMA-Fc groups along with the Fc and PBS control groups.

hBCMA-fc-300				hBCMA-100				hBCMA-Fc-30			
Mouse#	%CD4	%CD8	%B220		%CD4	%CD8	%B220		%CD4	%CD8	%B220
1.0	16.3	11.0	16.4	5.0	26.1	14.9	10.1	9.0	2.5	6.9	10.3
2.0	24.1	11.1	11.6	6.0	21.1	11.3	10.6	10.0	13.2	5.2	23.4
3.0	18.2	7.4	9.9	7.0	24.6	13.3	8.3	11.0	15.9	6.4	29.2
4.0	25.4	13.3	13.1	8.0	20.0	11.3	13.4	12.0	14.8	7.6	31.5
x	21.0	10.7	12.8	x	23.0	12.7	10.6	x	11.6	6.5	23.6
sd	4.4	2.4	2.8	sd	2.9	1.7	2.1	sd	6.2	1.0	9.5
Fc				PBS							
33.0	7.0	8.1	25.4	37.0	16.9	8.3	15.5				
34.0	10.7	4.9	15.3	38.0	19.1	12.1	19.5				
35.0	18.9	9.3	21.0	39.0	7.1	3.4	17.5				
36.0	20.1	11.1	21.0	40.0	19.9	11.4	26.5				
x	14.2	8.4	20.7	x	15.8	8.8	19.8				
sd	6.4	2.6	4.1	sd	5.9	4.0	4.8				

**Figure 36: Specific APRIL binding to Human Cell lines
determined by FACS analysis**

APRIL binding

HT 29 Colon adenocarcinoma	++
NCI 460 Lung carcinoma	++
PC3 Prostate adenocarcinoma	++
C6 Glial carcinoma	++
Raji Burkitt lymphoma	++
A20 Mouse B cell lymphoma	++
U266BI Myeloma	++
A435 Epidermoid carcinoma	--
A469 Kidney carcinoma	--
MDA-231 breast adenocarcinoma	--

Figure 37: Effect of APRIL, BCMA-Fc and TACI-Fc truncated on U266BI cell proliferation

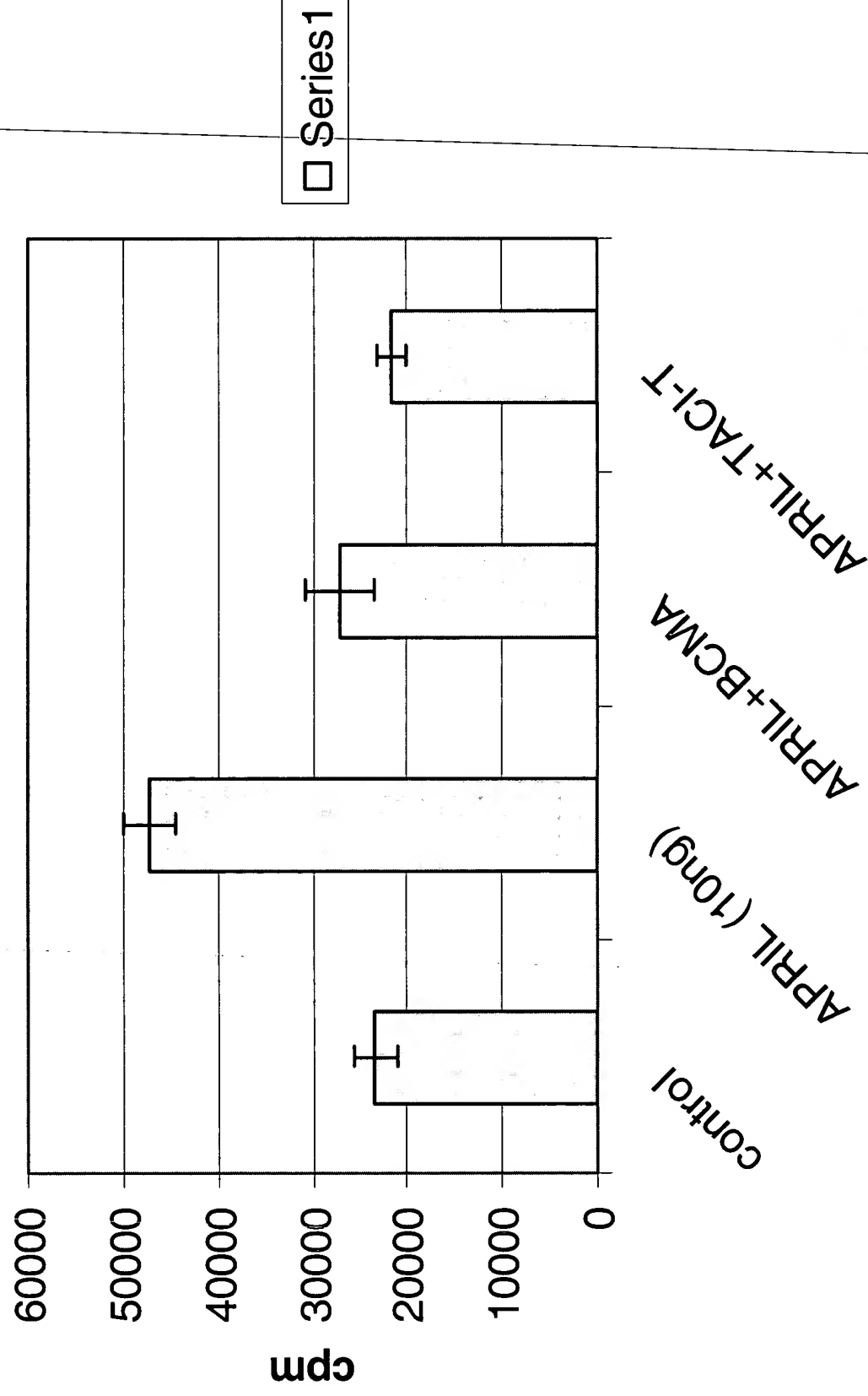


Figure 38: APRIL and AGP3 stimulates and BCMA-Fc inhibits B lymphoma cell proliferation

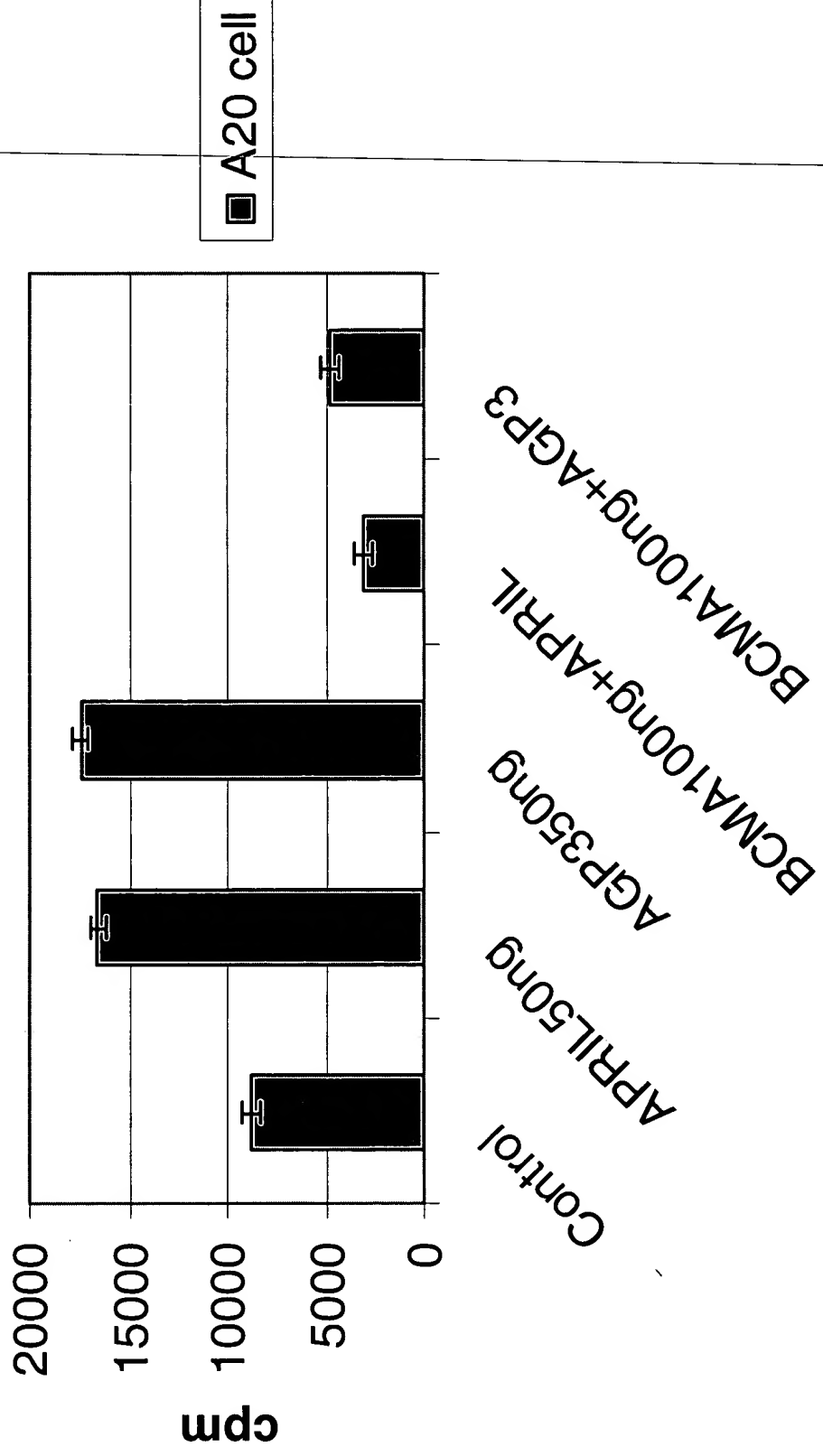
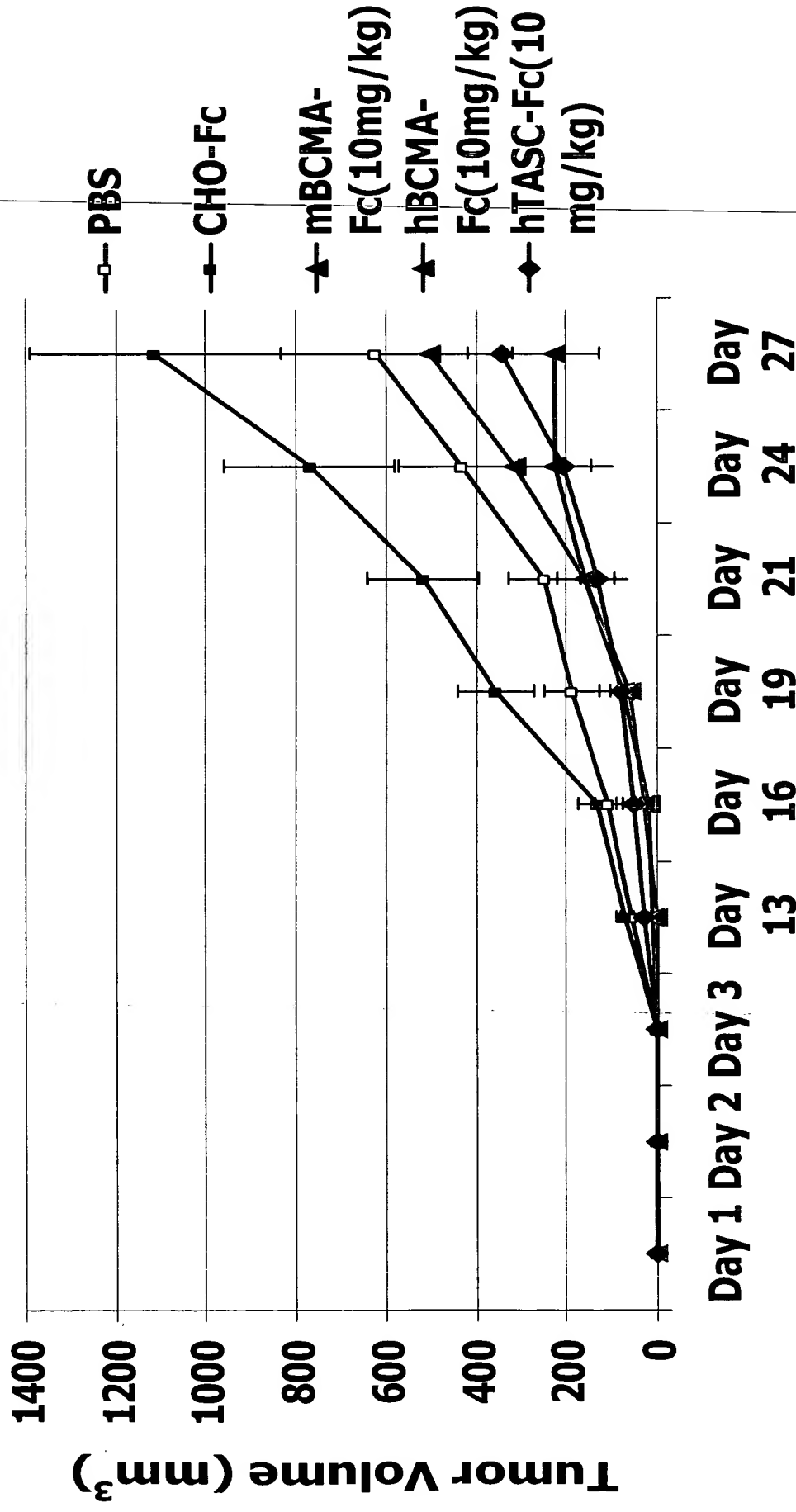


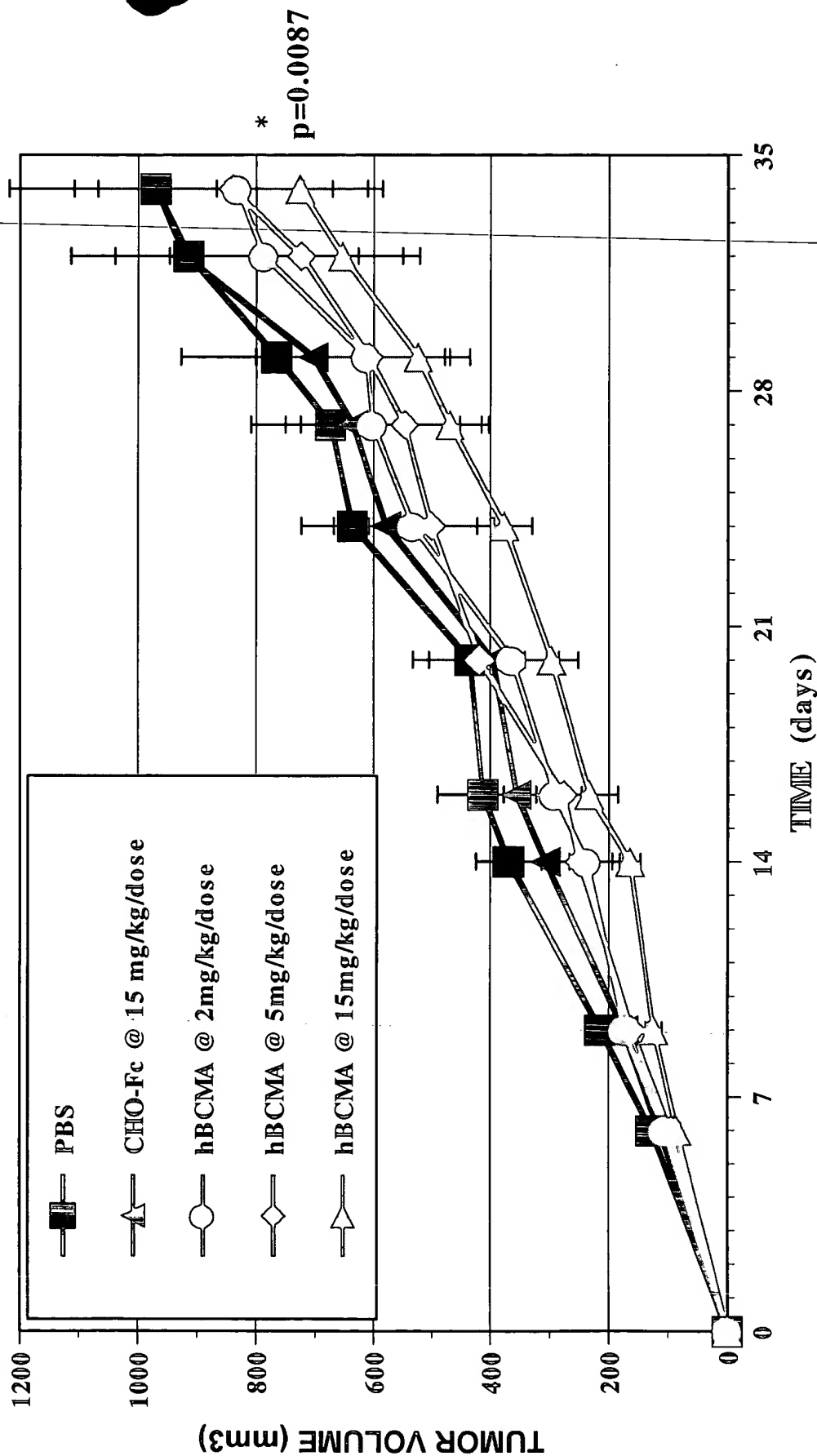
Figure 39: Effects of BCMA & hTACI on the Growth of A20 in Balb/c Mice



Days After Tumor Implantation

EFFECT OF HUMAN BCMA-Fc AGAINST HT-29 SC TUMOR GROWTH

Rx: IP, Q2D, day 0

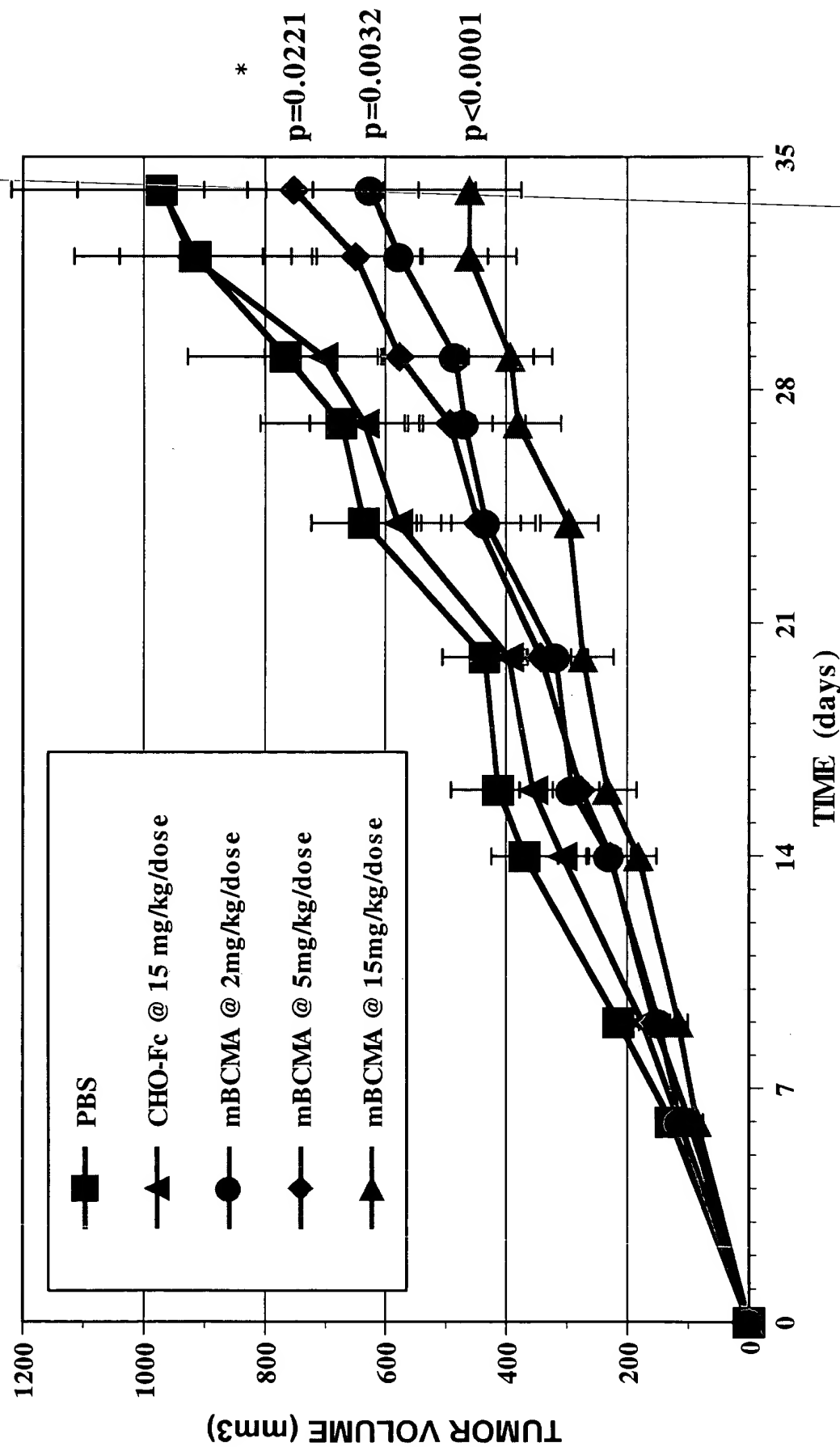


* Linear growth ANOVA with Dunnett's correction for multiple testing (n=10/group)

Figure 41

EFFECT OF MURINE BCMA-Fc AGAINST HT-29 SC TUMOR GROWTH

Rx: IP, Q2D, day 0



* Linear growth ANOVA with Dunnett's correction for multiple testing (n=10/group)